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14. ABSTRACT

The purpose of the research is to characterize patterns of care, utilization, and outcomes of treatments for localized prostate cancer such as surgery, external beam radiation, and brachytherapy. In particular, the research characterizes the patterns of care, utilization and outcomes of minimally invasive radical prostatectomy (MIRP) versus open retropubic radical prostatectomy (RRP). MIRP utilization increased from 9% to 43% from 2003 to 2007. Lengths of stay, transfusions, and stricture rates are lower for MIRP vs. RRP. However, erectile dysfunction and incontinence were more frequently diagnosed postoperatively. Additionally positive surgical margins were similar by surgical approach. While higher RRP surgeon volume was associated with fewer complications, this was not observed for MIRP surgeon volume and outcomes. In addition, MIRP was $293 more costly than RRP. Finally, pelvic lymph node dissection was performed less frequently with MIRP vs. RRP.

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I Introduction

The objective of this 4-year study is to characterize the use and outcomes of competing therapies for treating localized prostate cancer. Moreover, this project will evaluate utilization trends, patterns of care, costs and outcomes of minimally invasive radical prostatectomy (MIRP), i.e. laparoscopic radical prostatectomy (LRP) and robotic assisted laparoscopic radical prostatectomy (RALP), compared to open radical prostatectomy (ORP), external beam radiotherapy (XRT), and brachytherapy (BRCY). The findings of this project will guide men with prostate cancer weighing treatment options, employers and policy makers implementing healthcare coverage, and providers seeking to deliver cost-effective, high quality care. This project will be the first national, population-based study to evaluate patterns of care and outcomes for treatments of localized prostate cancer in a wide range of health care settings. In particular, we will assess the impact of LRP, RALP, XRT, and BRCY provider volume on complications, health-related quality of life, and cancer control.

Body

Perineal versus Minimally Invasive and Open Retropubic Radical Prostatectomy

In our analyses of MIPR vs. RRP, which showed rapid adoption of MIRP and fewer transfusions, strictures, and shorter length of stay for MIRP vs. RRP[1], we excluded men undergoing perineal radical prostatectomy (PRP) due to it becoming a infrequently use open surgical approach. For much of the 20th century, PRP was the predominant surgical approach; however, sampling pelvic lymph nodes involved a separate incision during PRP and urologists were using a lower midline for bladder, ureteral, and other pelvic surgeries more frequently. This led to a shift away from the perineal approach to the open retropubic approach, and due to loss of familiarity, PRP currently has a very prolonged learning curve. However, one could argue that minimally invasive approaches to radical prostatectomy have a very prolonged learning curve as well. The purpose of our population-based study was to compare cost and outcomes for PRP vs. RRP and MIRP.

We identified men who underwent PRP (n=452), MIRP (n=1,938), and RRP (n=6,899) during 2003 to 2007 from SEER-Medicare linked data, and PRP comprised 4.9% of the radical prostatectomies during the study period (Figure 1).[2] In propensity-score adjusted analyses, men undergoing PRP vs. RRP experienced shorter hospitalizations (median 2 vs. 3 days, $p<0.001$), fewer heterologous transfusions (7.2% vs. 20.8%, $p<0.001$), and required less additional cancer therapy (4.9% vs. 6.9%, $p=0.020$). When comparing PRP vs.

MIRP, men undergoing PRP required more heterologous transfusions (7.2% vs. 2.7%, p=0.018), but experienced fewer miscellaneous medical complications (5.3% vs. 10.0%, p=0.045). The median expenditures (Table 1) for PRP, RRP, and MIRP were $11,019, $12,767, and $13,335 in the first six months post-operatively; therefore PRP cost $2,000 less than either RRP or MIRP (p<0.001).

This is the first population-based study comparing all 3 surgical approaches to radical prostatectomy, and despite its decreasing utilization in a nationally representative cohort in the last decade, PRP has equivalent or improved 30-day and intermediate and long-term outcomes compared with both open radical retropubic and minimally-invasive approaches to radical prostatectomy. With increased scrutiny on medical costs and comparative effectiveness, it appears that PRP offers an excellent option in the armamentarium of the urologist in treatment of prostate cancer. However, the decreasing utilization and lack of familiarity with this procedure in modern practice may limit the future application of this cost-effective and oncologically-sound approach to radical prostatectomy.

Population-Based Determinants of Positive Surgical Margins

A measure of cancer control during radical prostatectomy is the likelihood of cancer at the edge of the specimen, or a positive surgical margin PSM. There are few comparisons of MIRP vs. RRP PSMs, and we used a population-based approach employing SEER-Medicare data to assess factors associated with PSMs.[3] Overall, 19.4% of men experienced PSMs with a pT2 vs. pT3a PSM rate

of 14.9% vs. 42% (p<0.001). Extrapolating from our population-based results, a surgeon incurring more than 3 PSMs in 10 cases of pT2 disease performed below the 25th percentile (Table 2). Additionally, there was a trend for fewer PSMs with minimally invasive vs. open RP (17.4% vs. 20.1%, p=0.086), and the PSM rate also decreased over the study period from 21.3% to 16.6% in 2004 vs. 2006 (p=0.028) with significant geographic variation (p<0.001). In adjusted analyses (Table 3), temporal and geographic variation in PSM persisted, and men with high (OR3.68, 95%CI 2.82-4.81) and intermediate (OR 2.52, 95%CI 2.03-3.13) vs. low-risk disease were at greater odds to experience PSMs. Notably, neither surgical approach nor surgeon volume was significantly associated with PSMs.

Our population-based PSM benchmarks allow identification of under-performing outliers who may seek courses or video self-study to improve outcomes. While there was significant temporal and geographic variation in PSMs, neither surgeon volume nor surgical approach was associated with PSMs. This is the first population-based study of PSMs during radical prostatectomy, which increases the likelihood of cancer recurrence and need for additional cancer therapies. In addition, we derived a means of identifying surgeons performing at or below the 25th and 10th percentiles, which may serve as a quality indicator for surgeons performing radical prostatectomy.

Utilization and Expense of Additional Cancer Therapies Following Radical Prostatectomy

In assessing characteristics associated with the use of additional cancer therapies such as radiation and/or hormones after radical prostatectomy, we used SEER-Medicare data from 2004-2006 to identify 4,247 men who underwent RP, of whom 600 subsequently received adjuvant therapies.[4] We used Cox regression to identify factors associated with receipt of adjuvant therapies and estimate healthcare expenditures within 12 months of diagnosis were compared for RP alone vs. RP and adjuvant therapies. Biopsy Gleason score, PSA, risk group and SEER region were significantly associated with receipt of adjuvant treatments (all $p<0.001$). Higher surgeon volume was associated with lower odds of receiving adjuvant therapies (hazard ratio [HR], 0.60; 95%CI, 0.46-0.78 [$p<0.001$]). Factors associated with receipt of adjuvant therapies (Table 4) were positive surgical margins (HR, 3.02; 95% CI, 2.55-3.57 [$p<0.001$]), high risk group vs. low (HR, 7.65; 95% CI, 5.64-10.37 [$p<0.001$]), lymph node positive disease (HR, 5.36; 95% CI, 3.71-7.75 [$p<0.001$]) and treatment in Iowa (HR, 1.93; 95%CI, 1.12-3.32 [$p=0.019$]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95%CI, 1.09-3.39 [$p=0.025$]) vs. San Francisco SEER regions. Age, race, comorbidities, and surgical approach were not associated with use of adjuvant therapies. The median expenditures attributable to post-prostatectomy hormonal therapy, radiation therapy, and radiation with hormonal therapy vs. were $3,697, $17,290, and $29,385 (Table 5).

Men treated by high volume surgeons were less likely to receive adjuvant therapies. Regional variation and high-risk disease characteristics were associated with increased receipt of adjuvant therapies, which increased health

expenditures by 2-3 fold when radiotherapy was administered. This study reinforces the importance of limiting positive surgical margins, which increase the cost of treating prostate cancer if adjuvant or salvage radiation or hormone therapy is added.

Higher RRP surgeon volume is associated with lower complications and shorter lengths of stay. However, the effect of MIRP surgeon volume on outcome is less clear. Therefore we performed a population-based study to determine the effect of MIRP surgeon volume on outcomes, and correlate with those of RRP surgeon volume-outcomes.

Cost Implications for the Rapid Adoption of New Technologies to Treat Prostate Cancer

For radiation treatment of prostate cancer, intensity modulated radiation therapy (IMRT), a more costly treatment option compared to standard conformal radiation therapy (CRT), has been rapidly adopted with little evidence similar to MIRP for surgery. However, the cost implications for the rapid adoption of these technologies remains unclear in the U.S. health care system, which is saddled with spiraling health care costs and calls for reform. Using SEER–Medicare linked data, we determined treatment patterns for 45,636 men aged ≥65 years who received definitive surgery or radiation for localized prostate cancer diagnosed from 2002-2005.[5] We calculated costs attributable to prostate cancer as the difference in Medicare payments in the year following vs. the year prior to diagnosis, and all costs were standardized to 2008 dollars. Of the study cohort, 26% received surgery, 38% external bean radiotherapy, and 36% brachytherapy.

Among surgical patients, MIRP utilization increased substantially (1.5% among 2002 diagnoses vs. 28.7% among 2005 diagnoses, $p<0.001$). For radiotherapy, IMRT utilization increased substantially (28.7% vs. 81.7%, $p<0.001$) and for men receiving brachytherapy, supplemental IMRT increased significantly (8.5% vs. 31.1%, $p<0.001$). The mean incremental cost of IMRT vs. 3D-CRT was $10,986; of brachytherapy + IMRT vs. brachytherapy+3D-CRT was $10,789; of MIRP vs. open RP was $293. Extrapolating these figures to the total U.S. population results in excess spending of $282 million for IMRT, $59 million for brachytherapy+IMRT, and $4 million for MIRP, compared to less costly alternatives for men diagnosed in 2005.

Costlier prostate cancer therapies were rapidly and widely adopted, resulting in an excess national spending of over $350 million among men diagnosed in 2005 and suggesting the need for comparative effectiveness research to weigh their costs against their benefits, as there is little level I evidence, or population-based comparisons of these treatment modalities.

Overuse of Imaging to Stage Low-Risk Prostate Cancer

In assessing patterns of care for men with prostate cancer, we also examined factors associated with the use of pretreatment imaging for men with low-risk prostate cancer. At present, pre-treatment imaging is only recommended for high-risk prostate cancer by the American Urological Association and the National Comprehensive Cancer Network, as there is a less than 1% risk for a positive bone scan or computerized tomography (CT) scan. Using SEER-

Medicare data from 2004-2005, we identified 6,444 men low with low-risk prostate cancer, and 2,330 (36.2%) underwent imaging studies; 1512 (23.5%), 1710 (26.5%), and 118 (1.8%) men underwent cross-sectional imaging (CT or MRI), bone scan, and abdominal ultrasound, respectively.[6] Radiation therapy vs. surgery was associated with greater odds of imaging (Odds Ratio [OR], 1.99; 95% CI, 1.68-2.35 [p<0.01]). While active surveillance vs. surgery was associated with lower odds of imaging (OR, 0.44; 95% CI, 0.34-0.56 [p<0.01]). Factors associated with increased odds of imaging were median household income > $60,000 (OR, 1.41; 95% CI, 1.11-1.79 [p<0.01]), and men from New Jersey vs. San Francisco (OR, 3.11; 95% CI 2.24-4.33 [p<0.01]) experienced greater odds of imaging. Men living in areas with >90% vs. <75% high school education experienced lower odds imaging (OR, 0.76; 95% CI, 0.6-0.95 [p=0.02]). There is widespread overutilization and significant geographic variation for use of imaging to stage low-risk prostate cancer. Moreover, treatment associated variation in imaging was noted with the greatest vs. lowest imaging utilization observed for radiation therapy vs. active surveillance.

Inappropriate utilization of radiographic imaging in men with newly diagnosed prostate cancer

The American Urological Association issued Best Practice Statements in 2000 and 2009 recommending pretreatment staging of prostate cancer only in the setting of high-risk disease.[7] These statements used PSA, Gleason grade at biopsy and clinical stage to predict the yield of imaging studies. Radiographic imaging is also recommended only in the setting of high-risk clinical features by

the National Comprehensive Cancer Network (NCCN).[8] Other professional societies involved in the management of prostate cancer (e.g. American Society of Clinical Oncology, American Society for Therapeutic Radiology and Oncology and the American Cancer Society) do not have specific recommendations for utilization of post-diagnosis radiographic screening.

The goals of this study were to: 1) characterize utilization patterns for diagnostic imaging relative to established guidelines; and 2) estimate the cost of imaging overutilization.

the study cohort of 30,183 men was stratified into risk groups according to clinical stage, preoperative PSA, and Gleason grade based on NCCN practice guidelines.[8]

Outcomes

The primary outcome was utilization of radiographic staging studies (CT, MRI or bone scan) prior to the start of treatment. Intensity-modulated or conformal external beam radiation therapy and interstitial brachytherapy were considered jointly as standard radiation therapies, while proton beam therapy was considered separately. Pre-treatment imaging for radiation planning was identified by corresponding CPT-4 codes and excluded from analysis. Men who did not undergo definitive therapy more than one year after diagnosis were categorized as active surveillance.

To best attribute the cost associated with radiology services, we assessed Medicare payments from outpatient claims. The estimated cost per additional

study was estimated as the sum of the median expenditure per claim from the outpatient and carrier files. Assuming that 32% and 43% of the 462,200 men with newly diagnosed prostate cancer in 2004 and 2005 were low- and intermediate–risk,[9] we extrapolated the cost of imaging studies nationally as previously described.[5]

In 2004 and 2005, 9,640 (32%) men were diagnosed with low-risk prostate cancer, while 12,966 (43%) and 7,577 (25%) men had intermediate- and high-risk disease, respectively (Table 6). Thirty six percent, 49% and 61% of low-, medium- and high-risk patients, respectively, underwent radiographic imaging during the interim between diagnosis and treatment initiation. Bone scan was the most common test used in all three risk strata, and greater utilization of all three imaging modalities was observed with increasing risk (Figure 2).

Men with low-risk prostate cancer were more likely to be younger, white, reside in urban areas and have fewer comorbidities than men with intermediate- and high-risk disease ($P<0.001$ for all). Men with high-risk disease were more likely to be unmarried and had lower education levels and household incomes compared to men with lower risk prostate cancer ($P<0.001$ for all). Men with intermediate-risk disease were more likely to undergo radical prostatectomy compared to men with either low- or high-risk disease, while men with low-risk disease were most likely to opt for active surveillance ($P<0.001$). Treatment with androgen deprivation therapy (ADT) alone was most likely among men with high-risk disease while standard radiation therapies were less likely with more aggressive tumor characteristics ($P<0.001$). In the high-risk cohort (Figure 3), 59% versus 79% of

men underwent imaging prior to radical prostatectomy versus standard radiation therapies (P<0.001).

In adjusted analyses (Table 7), men aged greater than age 70 were more likely to undergoing imaging compared with men aged 65 to 69 years (age 70-74: OR 1.10, 95% CI 1.03-1.17, P=0.003; age 75 or greater: OR 1.25, 95% CI 1.17-1.33, P<0.001). Black men were more likely (OR 1.11, 95% CI 1.01-1.21, P=0.031) to undergo imaging than white men. Men residing in areas with higher education levels were less likely (>90% with high school education versus <75%: OR 0.84, 95% CI 0.76-0.92, P<0.001) to undergo imaging. Compared with men living in areas with median household income less than $35,000, men with median household incomes of $35,000 to 44,999 (OR 1.11, 95% CI 1.04-1.20, P=0.004), $45,000 to 59,999 (OR 1.09, 95% CI 1.0-1.19, P=0.038) or greater than or equal to $60,000 (OR 1.19, 95% CI 1.08-1.32, P<0.001) were more likely to undergo prostate cancer imaging. Moreover, men residing in rural versus urban areas were more likely (OR 1.22, 95% CI 1.11-1.34, P<0.001) to undergo imaging studies. Men undergoing ADT alone (OR 0.84, 95% CI 0.77-0.93, P<0.001) or active surveillance (OR 0.17, 95% CI 0.15-0.19, P<0.001) versus radical prostatectomy were less likely to undergo imaging. However, men treated with cryotherapy (OR 1.22, 95% CI 1.02-1.44, P=0.014), proton beam therapy (OR 1.56, 95% CI 1.21-1.99, P<0.001) or standard radiation therapies (OR 1.77, 95% CI 1.66-1.90, P<0.001) versus radical prostatectomy were more likely to undergo imaging studies.

Low-risk characteristics

Men living in areas with greater than 90% versus less than 75% high school education were less likely to undergo imaging (90% versus 75%, OR 0.77, 95% CI 0.64-0.93, P=0.006), whereas men living in areas with median annual household income greater than $60,000 had a higher likelihood of having a imaging study compared with those living in areas with median income less than $35,000 (OR 1.32, 95% CI 1.09-1.60, P=0.005). Compared with men undergoing radical prostatectomy, men undergoing cryotherapy (OR 1.44, 95% CI 1.06-1.98, P=0.022) or standard radiation therapies (OR 1.82, 95% CI 1.59-2.08, P<0.001) had greater odds of radiographic imaging while men managed with active surveillance had lower odds of imaging (OR 0.27, 95% CI 0.22-0.34, P<0.001).

Intermediate-risk characteristics

Men aged greater than 70 were more likely to undergo imaging compared to men aged 65 to 69 (versus age 70-74: OR 1.11, 95% CI 1.01-1.23, P=0.031; versus age 75 or greater: OR 1.14, 95% CI 1.02-1.26, P=0.016). Black men were more likely to undergo imaging (OR 1.15, 95% CI 1.0-1.33, P=0.047) compared with white men. Men who chose active surveillance were less likely (OR 0.23, 95% CI 0.18-0.28, P<0.001) to have an imaging test than those treated with radical prostatectomy. Men treated with cryotherapy (OR 1.27, 95% CI 1.0-1.62, P=0.049), proton beam therapy (OR 1.95, 95% CI 1.33-2.85, P<0.001) or standard radiation therapies (OR 1.90, 95% CI 1.72-2.11, P<0.001) were more likely to undergo imaging tests than men who had radical prostatectomy.

High-risk characteristics

Compared with men undergoing radical prostatectomy, men undergoing ADT alone (OR 0.62, 95% CI 0.51-0.74, P<0.001) or active surveillance (OR 0.16, 95% CI 0.12-0.21, P<0.001) were less likely to undergo imaging, whereas men treated with cryotherapy (OR 1.64, 95% CI 1.06-2.55, P=0.027), proton beam therapy (OR 2.13, 95% CI 1.1-4.12, P=0.025) or standard radiation therapies (OR 2.21, 95% CI 1.87-2.62, P<0.001) were more likely to have pre-treatment imaging.

Expenditures

The median Medicare payment for bone scan, CT and MRI was $226, $407 and $394, respectively. The total Medicare payment for imaging in men with low- and intermediate-risk prostate cancer in the study population was $3,874,681. Extrapolating from these results using the estimate of 462,200 new diagnoses of prostate cancer in the United States in 2004 and 2005, 86,981 CT scans, 11,893 MRI scans and 137,477 bone scans were performed on men with low- or intermediate-risk characteristics at a cost of $71,156,980.

There is widespread overutilization of imaging for low- and intermediate-risk prostate cancer, while a worrisome number of men with high-risk disease did not receive appropriate imaging studies to exclude metastases prior to therapy.

Trends in the Care of Radical Prostatectomy in the United States from 2003-2006

The utilization of nerve-sparing approaches in radical prostatectomy has improved postoperative morbidity and its dissemination over the past 20 years has shown a decrease in retropubic radical prostatectomy (RRP) postoperative morbidity over time.[10] While MIRP has not had a similar period to refine surgical technique, the intrinsic advantages of robotic-assistance (magnification, motion scaling and tremor filtration) have been argued to potentially provide superior technical reconstruction of the urethrovesical anastomosis and nerve-sparing and subsequently improve perioperative and postoperative outcomes. While the two approaches have been previously compared in single institution settings, we sought to assess this hypothesis by evaluating temporal trends between the varying surgical approaches nationally in a community setting.[11]

We identified a population of 19,542 men with newly diagnosed prostate cancer by the International Classification of Disease, Ninth Revision ICD-9 code (185.0). Data used for the analysis were derived from the MarketScan® Commercial Claims and Encounters (CCAE) and the Medicare Supplemental and Coordination of Benefits database to longitudinally assess the inpatient and outpatient experience for men after definitive prostate cancer surgery from 2003 to 2006. These databases incorporate the health services of approximately 3 million employees, dependents, and retirees in the United States with primary or Medicare supplemental coverage through privately insured fee-for-service, point of service, or capitated health plans. The MarketScan® CCAE and Medicare

supplemental databases are generally representative of the demographic makeup of the United States, although higher concentrations of MarketScan® patients reside in the South and Midwestern areas of the United States than the general population.

We captured variables of interest using relevant ICD-9 or CPT-4 diagnosis and procedure codes.[1] Hospital length of stay (LOS) was defined as the number of days from admission to discharge during the initial surgical visit. Heterologous blood transfusions were included if they occurred during the surgical hospital admission. Perioperative complications were ascertained in the 30 days after surgery and included potentially life-threatening cardiac, respiratory, or vascular events; bleeding; and other events, such as renal failure and shock. Additionally, a MarketScan® variable for death was assessed within 30-days of radical prostatectomy. Patients who underwent a reoperation within the first postoperative week were also examined. Anastomotic strictures were identified up to 6 months after surgery.[1] Incision hernia repair was assessed in the year following radical prostatectomy.

Utilization rates for PRP, RRP, and MIRP were examined from 2003 to 2006. We compared trends in patient characteristics and outcomes of interest by surgical approach through the study period using Cochran-Armitage trend tests, and univariate differences between treatment modalities were assessed with chi-square tests. Mean LOS was compared with one-way analysis of variance; the Wilcoxon rank sum-test gave similar results, so for simplicity, we present the ANOVA. All analyses were performed in SAS 9.2 (SAS Institute, Cary, NC).

Surgical utilization rates for MIRP increased from 5.7% in 2003 to 39.2% in 2006, while RRP and PRP decreased from 89.1 to 57.3%, and 5.3 to 3.5%, respectively. Because PRP represented a small proportion of overall surgeries, we excluded patients undergoing PRP from further analysis, leaving a final sample size of 18,717.

Demographic data for patients undergoing MIRP and RRP are shown in Table 8. While the majority of individuals are between 55 to 65 years of age, the MIRP population tended to be slightly younger than the RRP cohort ($p<0.0001$). There was geographic variability between the two groups, with MIRP more likely to be performed in the Midwest and RRP more likely to be performed in the South. There were no differences in preoperative comorbidity between the two surgical approaches. Because of these differences in region and age in the two treatment groups, we also performed analyses for the outcomes adjusted for region and gender, but the results were similar to the unadjusted results, so for simplicity, we present unadjusted results for the outcomes.

Over the 4-year period, the mean and median LOS declined for patients undergoing MIRP ($p<0.0036$, Table 9). Overall perioperative complications decreased from 13.8% to 10.7% ($p=0.0233$). This finding was driven by the reduction in genitourinary (3.3 to 2.5%, $p<0.0488$) and miscellaneous surgical complications (3.6 to 2.3%, $p=0.0064$). Over the study period, there was a decrease in iatrogenic intestinal injury (1.5 to 0.1%, $p=0.0086$). Decreases in iatrogenic rectal injury repair (1.5 to 0.5%), surgical re-exploration within 30 days

of initial surgery (1.8 to 0.7%) and stricture formation (6.8 to 6.0%) were identified, but were not statistically significant.

Over the same study period, mean LOS for patients undergoing RRP decreased from 3.2 to 2.9 days, (p=0.0003) and overall perioperative complications decreased from 18.1% to 14.6%, (p=0.0070, Table 10). This decrease in perioperative complications was due to reductions in wound/bleeding complications, (2.0 to 1.1%, p=0.0022). No significant trend was seen in either MIRP or RRP groups for the rate of stricture formation or incisional hernia repair.

When comparing perioperative outcomes by surgical approach (Table 11), patients undergoing MIRP vs. RRP had a shorter mean hospital stay (1.8 vs. 3.1 days, p<0.0001). Additionally, patients undergoing MIRP experienced a reduced overall perioperative complication rate (12.5 vs. 17.1%, p<0.0001). This difference was statistically significant for cardiac (0.9 vs. 1.6%), respiratory (2.3 vs. 4.4%), vascular (1.3 vs. 2.1%), wound (1.0 vs. 1.5%), miscellaneous medical (4.4 vs. 5.8%) and miscellaneous surgical (3.3 vs. 4.1%) complications. The rate of blood transfusions (1.5 vs. 8.7%, p<0.0001) and anastomotic strictures (6.3 vs. 12.8%, p<0.0001) were lower for patients undergoing MIRP vs. RRP. Although stricture rates were lower in patients undergoing MIRP vs. RRP, postoperative use of cystography was higher (35.7 vs. 9.1%, p<0.0001) in those who underwent MIRP. Finally there were two 30-day postoperative RRP deaths in 2004 and 1 death in 2006 while there were no deaths within 30 days of MIRP during the study period.

The increasing adoption of minimally-invasive approaches to radical prostatectomy during the mid-decade has been associated with reductions in hospital stay, perioperative complications, and iatrogenic injuries. Additionally, the complication rate is lower during MIRP than for patients undergoing RRP over the same period. While individual physician practice patterns may influence lengths of stay and patient selection, increasing utilization of MIRP has continued to reduce the morbidity associated with radical prostatectomy nationally.

Comparison of Outpatient Narcotic Prescribing Patterns after Minimally Invasive vs. Retropubic and Perineal Radical Prostatectomy

Theoretically, MIRP vs. RRP and perineal radical prostatectomy (PRP) is associated with less postoperative pain due to smaller incisions and reduced traction on abdominal wall musculature. However, few studies have compared longer-term objective outpatient narcotic requirements following RP, and extended postoperative pain may be a societal burden as men may require more time away from work. Using a population-based approach, we compared outpatient narcotic prescription utilization for MIRP, RRP, and PRP.[12]

We identified 31,729 men diagnosed with prostate cancer during 2003-2006 from Medstat MarketScan® using the International Classification of Disease, Ninth Revision (ICD-9) code 185.0. MarketScan® incorporates the health services of approximately 3 million employees, dependents, and retirees in the United States with primary or Medicare supplemental coverage through privately insured fee-for-service, point of service, or capitated health plans. MarketScan® is generally

representative of the demographic makeup of the U.S., although more subjects reside in the South and Midwest than the general population. Men who underwent PRP, RRP, or MIRP (i.e. laparoscopic with or without robotic assistance) were identified using the Current Procedural Terminology, Fourth Edition (CPT-4) codes: 55810, 55812, 55815 for PRP; 55840, 55842, 55845 for RRP; and 55866 for MIRP.

Many private payers do not contribute outpatient prescription data, thus to ensure that we captured narcotic prescription utilization specific to post-prostatectomy pain we limited the cohort to those subjects filling a narcotic prescription within 7 days of discharge. Subjects were also censored if they changed health plan coverage within 90 days surgery in order to capture complete follow-up. Following censoring, the final cohort consisted of 10,706 men (2206 MIRP, 8037 RRP, and 463 PRP).

Outpatient narcotic prescription utilization up to 90 days before and after RP was identified using the Food and Drug Administration designated National Drug Codes (NDC) for oral narcotics, yielding the following medications: codeine, hydrocodone, hydromorphone, meperidine, morphine, MS Contin, oxycodone, oxycontin, pentazocine, propoxyphene, and tramadol. In order to assess the various strengths, types, and amount of postoperative narcotic use, the cumulative morphine sulfate equivalent (MSe) was derived (Appendix). Distributions were non-normal and therefore medians were compared by surgical approach.

Age at diagnosis (<55, 55-64, 65-74, >75 years), comorbidities using the Charlson index derived from healthcare encounters the year prior to prostatectomy,[13] health plan type (Comprehensive, Health Maintenance Organization [HMO], Preferred Provider Organization [PPO], Point of Service [POS] or other) and geographic region classified according to US Census Bureau regions (Northeast, Midwest, South, West) were obtained from the enrollment file.

Demographic characteristics and narcotic utilization patterns including total narcotic prescription MSe, number of refills required, and total narcotic prescription cost were compared with Pearson chi-square testing. Analgesic costs were derived as total primary health plan expenditures for narcotics within 90 days of surgery, excluding insurance deductibles, co-payments and other third party payments from supplemental insurances. Multivariate models were constructed to determine the effect of surgical approach, age, comorbidity, geographic region, health plan type, and baseline narcotic use on postoperative outpatient MSe use, refills, and costs.

Demographic characteristics of the study population are shown in Table 12. Men undergoing MIRP were younger ($p=0.002$) while men undergoing RRP had fewer comorbidities ($p=0.005$). Men with HMO coverage were less likely to undergo MIRP while those with PPO coverage were more likely to undergo MIRP ($p<0.001$). MIRP was more commonly performed in the Midwest, while RRP and PRP were most commonly performed in the South ($p<0.001$). There were no differences in baseline preoperative narcotic utilization by surgical approach.

Postoperatively, MIRP was associated with lower median total narcotic strength consumption vs. RRP and PRP (6.7 vs. 6.9 and 8.3 MSe, p<0.001, Figure 4). Similarly, fewer additional narcotic refills were associated with MIRP vs. RRP and PRP (20.2% vs. 28.9% and 42.3%, p<0.001, Table 13). Correspondingly, lower median narcotic costs were associated with MIRP vs. PRP and RRP ($8 vs. $10 and $10, p<0.001.

In adjusted analyses (Table 14), PRP (RR 1.11, 95% CI 1.03-1.21, referent RRP), younger age (<55 years, RR 1.22 95% CI 1.04-1.43; age 55-64 years, RR 1.17 95% CI 1.00-1.37, referent >75 years) and baseline narcotic use (RR 2.70 95% CI 2.56-2.84) were associated with greater MSe consumption. Although MIRP was not associated with differences in MSe consumption vs. RRP, MIRP was associated with fewer narcotic refills (OR 0.6, 95% CI 0.54-0.69) and lower narcotic prescription costs (RR 0.94, 95% CI 0.90-0.98). Similar to MSe consumption, younger age (<55 years old, OR 2.22 95% CI 1.38-3.59; 55-64 years, OR 1.66 95% CI 1.04-2.67) and baseline narcotic use (OR 2.85, 95% CI 2.50-3.25) were associated with additional narcotic refills. Paralleling determinants of MSe use, PRP (RR 1.16, 95% CI 1.08-1.26), younger age (<55 years, RR 1.48 95% CI 1.26-1.73; 55-64 years, RR 1.34 95% CI 1.15-1.57) and baseline narcotic use (RR 3.00, 95% CI 2.85-3.15) were associated with higher narcotic prescription costs. Significant geographic variation was observed for MSe consumption, narcotic refills, and narcotic prescription costs.

Challenges of our research are as follows. First, we sought to differentiate robotic-assisted laparoscopic radical prostatectomy from standard laparoscopic

radical prostatectomy with use of the Healthcare Common Procedure Coding System (HCPCS) code S2900. However, our queries of SEER-Medicare data did not result in any men having this designation. We learned that Medicare does not reimburse a facility fee for use of the robot, and this may be why we have been unable to find this designation. We are currently using the Healthcare Costs and Utilization Project (HCUP) Nationwide Inpatient Sample to use the ICD-9 code 17.44, which was initiated on 10/1/08. Using NIS from the last quarter of 2008, we identified 2,348 robotic-assisted laparoscopic radical prostatectomy within the NIS, which after incorporating NIS survey weights, represented 11,513 robotic assisted laparoscopic radical prostatectomy. As the study period is one quarter of a year, annual procedure volumes were extrapolated by multiplying by 4 resulting in low, medium, high and very high volume quartiles corresponding to 14-60, 64-116, 120-216, and 240-664 RALP per year. Figure 1 shows the overall distribution of annual hospital RALP volume. We will assess whether higher robotic assisted laparoscopic radical prostatectomy volume is associated with better outcomes and lower costs.

The second challenge has been the evaluation of urinary continence and erectile dysfunction following treatments for localized prostate cancer. Originally, we proposed to conduct a survey of Medicare beneficiaries; however, the cost estimate from RESDAC underestimated the survey costs. Moreover, the limitations of a survey of Medicare beneficiaries are that we will not have designation of nerve-sparing or robotic-assistance for radical prostatectomy. Moreover, preservation of continence and potency are most challenging in men

aged 65 years and older. As an alternative approach, I contacted the New Jersey and Northern California Cancer SEER registries to perform a survey of men who were treated for prostate cancer in those regions. However, the budget for contacting and performing a survey of these men will be more expensive that the original budget. We will therefore compare the utilization, outcomes, and costs of incontinence and erectile dysfunction following treatments for localized prostate cancer using SEER-Medicare and NIS data.

Finally, current manuscripts include an assessment of the effect of surgeon and hospital volume on radical prostatectomy costs, a comparison of cryotherapy to brachytherapy, and characterizing patterns of care and outcomes of active surveillance and watchful waiting as compared to definitive therapies for localized prostate cancer. In addition, the most recent release of Medicare Part D data will allow us to assess the use of medications and associated costs following minimally invasive versus open radical prostatectomy. We are also conducting an analysis of cryotherapy as a treatment option for prostate cancer compared to ablative therapies such as brachytherapy. Finally, we are comparing different forms of radiation therapy (proton beam therapy, brachytherapy, external beam radiotherapy) with surgery

Key Research Accomplishments

- The majority of Specific Aim 1 has been completed: To evaluate utilization trends and patterns of care for minimally invasive radical prostatectomy. We have characterized the increased utilization of minimally invasive radical prostatectomy using SEER-Medicare[1,2] and Marketscan Medstat,[12,14] as we aimed to do. In addition, we are presently exploring temporal trends and patterns of care using a 100% Medicare sample, working with the Centers for Medicare and Medicad, as well as the Nationwide Inpatient Sample. We have found that Asians and those living in areas of greater income and education are drawn to minimally invasive vs. open radical prostatectomy.[1]
- The majority of Specific Aim 2 has been completed, particularly for radical prostatectomy[1,2,11,15]: To identify and compare determinants of post-treatment outcomes and costs. We are presently comparing outcomes and costs following radiation therapies such as brachytherapy, intensity modulated radiotherapy, 3-dimensional conformal radiotherapy, and proton beam therapy. In addition, we are assessing the effect of surgeon and hospital volume on prostate cancer treatment costs. Manuscripts in both of these areas are being finalized for submission.
- As mentioned previously, due to the unanticipated expense of survey research, we are limited to using a population-based assessment of secondary data rather that conducting a survey to carry out Specific Aim 3: To identify and compare determinants of post-treatment health related

quality of life (sexual, urinary, and bowel function) and cancer control. However, using SEER-Medicare data, we have demonstrated that men undergoing MIRP vs. RRP are more likely to be diagnosed with erectile dysfunction and urinary incontinence, but the use of salvage therapies was similar regardless of surgical approach.[1] In addition, we are able to assess cancer control following radical prostatectomy by comparing surgical margin status, and we did not find differences in positive margins between MIRP and RRP.[3] We are currently comparing the use of salvage hormone therapies following different forms of radiation therapy using SEER Medicare data.

Reportable Outcomes

From May 1 2010 to April 30 2011, The Prostate Cancer Physician Training Award has resulted in publications:

1. Prasad SM, Gu X, Lavelle R, et al: Comparative effectiveness of perineal versus retropubic and minimally invasive radical prostatectomy. The Journal of urology 185:111-5, 2011
2. Williams SB, D'Amico AV, Weinberg AC, et al: Population-based determinants of radical prostatectomy surgical margin positivity. BJU international 107:1734-40, 2011
3. Williams SB, Gu X, Lipsitz SR, et al: Utilization and expense of adjuvant cancer therapies following radical prostatectomy. Cancer, 2011
4. Nguyen PL, Gu X, Lipsitz SR, et al: Cost implications of the rapid adoption of newer technologies for treating prostate cancer. Journal of Clinical Oncology. 29:1517-24, 2011
5. Choi WW, Williams SB, Gu X, et al: Overuse of imaging for staging low risk prostate cancer. The Journal of urology 185:1645-9, 2011
6. Kowalczy KJ, Weinburg AC, Gu X, Yu H, Lipsitz SR, Williams SB, Hu JC. Comparison of Outpatient Narcotic Prescribing Patterns after Minimally Invasive vs. Retropubic and Perineal Radical Prostatectomy. The Journal of urology, In Press.
7. Prasad SM, Gu X, Nguyen PL, Hu JC. Inappropriate utilization of radiographic imaging in men with newly diagnosed prostate cancer. Cancer, In Press.
8. Williams SB, Prasad SM, Weinberg AC, Shelton JB, Hevelone ND, Lipsitz SR, Hu JC. Trends in the care of radical prostatectomy in the United States from 2003 to 2006. BJU international. In Press.

In addition, 4 abstracts (numbers 77, 435, 159, and 1784) were presented at the

American Urologic Association in May 2011 in Washington D.C.

77 COMPARATIVE EFFECTIVENESS OF PERINEAL VERSUS RETROPUBIC AND MINIMALLY INVASIVE RADICAL PROSTATECTOMY. Prasad SM, Gu X, Lavelle R, et al:

435 INAPPROPRIATE UTILIZATION OF RADIOGRAPHIC IMAGING IN MEN WITH NEWLY DIAGNOSED PROSTATE CANCER. Sandip Prasad, Xiangmei Gu, Jim Hu

159 ADJUVANT VS. SALVAGE RADIATION THERAPY FOLLOWING PROSTATECTOMY FOR LOCALLY ADVANCED PROSTATE CANCER: RESULTS FROM SEER-MEDICARE. Keith J. Kowalczyk, Xiangmei Gu, Hua-yin Yu, Paul L. Nguyen, et al.

1784 COMPARATIVE EFFECTIVENESS OF ROBOTIC-ASSISTED, LAPAROSCOPIC AND OPEN RADICAL PROSTATECTOMY: Hua-yin Yu, Nathanael Hevelone, Stuart Lipsitz, Jim Hu

Conclusions

The study to date is the first population-based comparison of MIRP vs. RRP and PRP, and is the highest level of evidence, as randomized control trials are lacking and are unlikely to be performed. Despite the absence of firm evidence, men of greater education and income were more likely to undergo MIRP vs. RRP.. In addition, we present population-based surgeon PSMs to help identify underperforming surgeons and also characterize the increased cost associated with adjuvant or salvage hormonal therapy. Finally, we characterized the additional health care costs of rapid, unregulated adoption of MIRP and IMRT and the overutilization of imaging for men with low-risk prostate cancer and the overutilization of PLND during radical prostatectomy. These may serve as potential areas to greater educate physicians and to dis-incentivize unnecessary imaging studies and surgeries.

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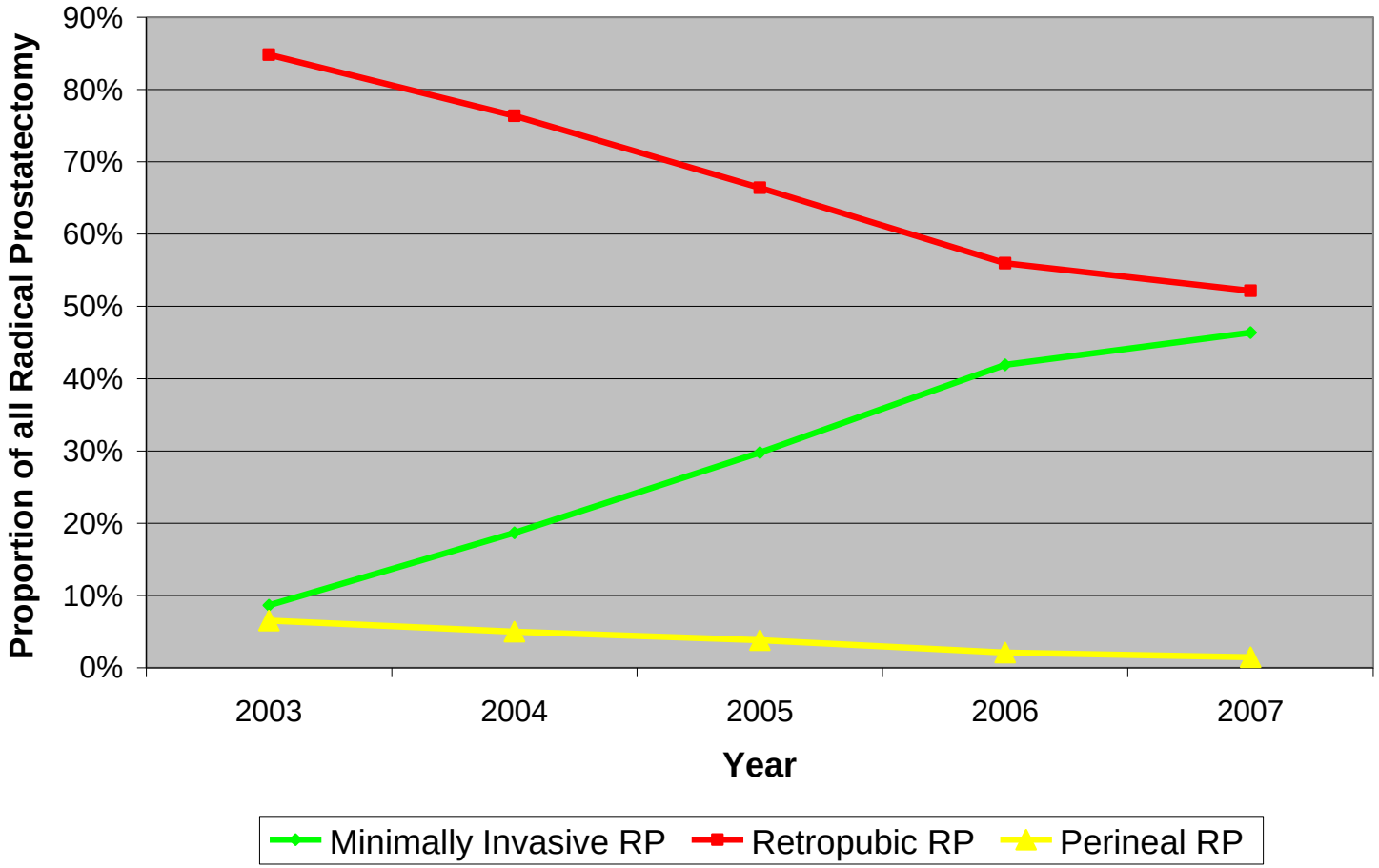

Figure 1. Radical prostatectomy by approach during study period

Figure 2: Test utilization by risk strata (P<0.001 in all groups between risk strata

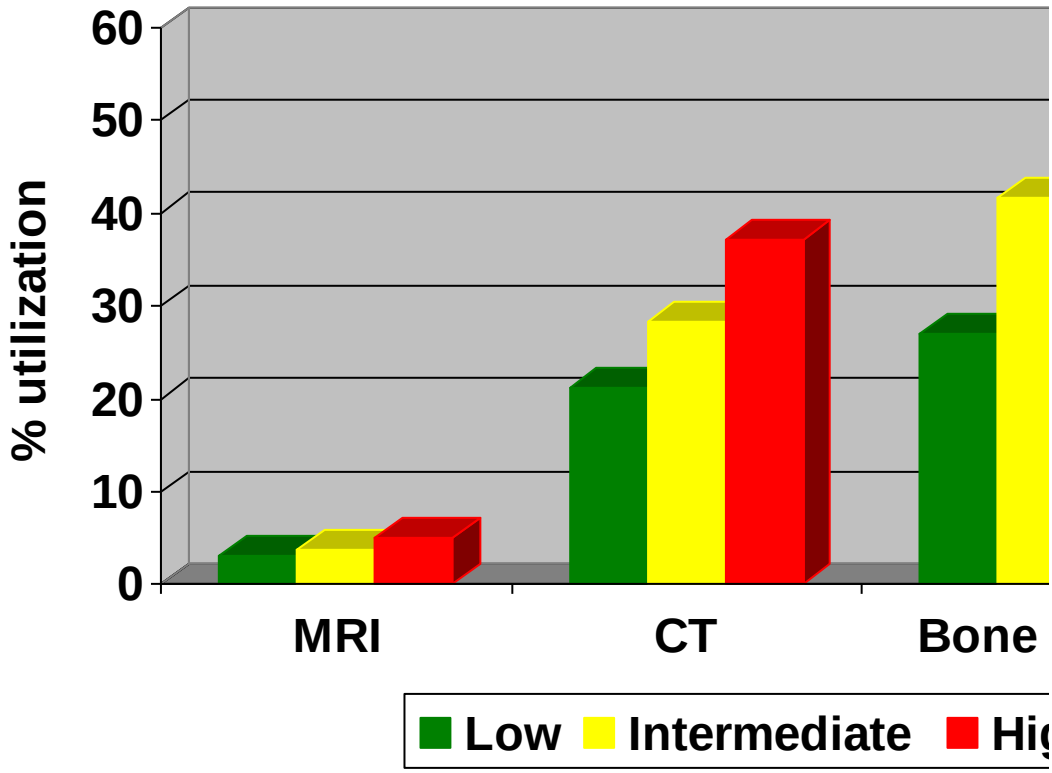

Figure 3: Test utilization by treatment type and risk group (P<0.05 in all groups between risk strata)

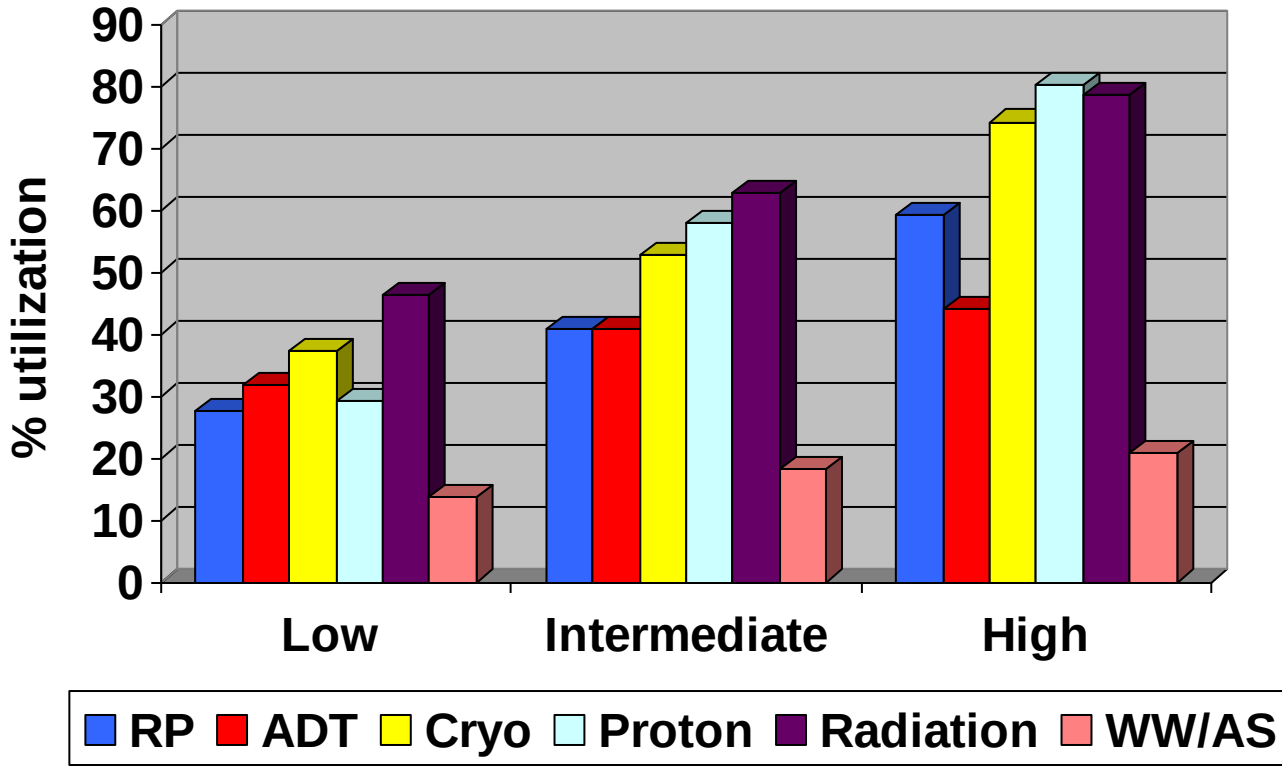

Figure 4. Univariate model comparing total strength of postoperative narcotic in MSe by surgical approach.

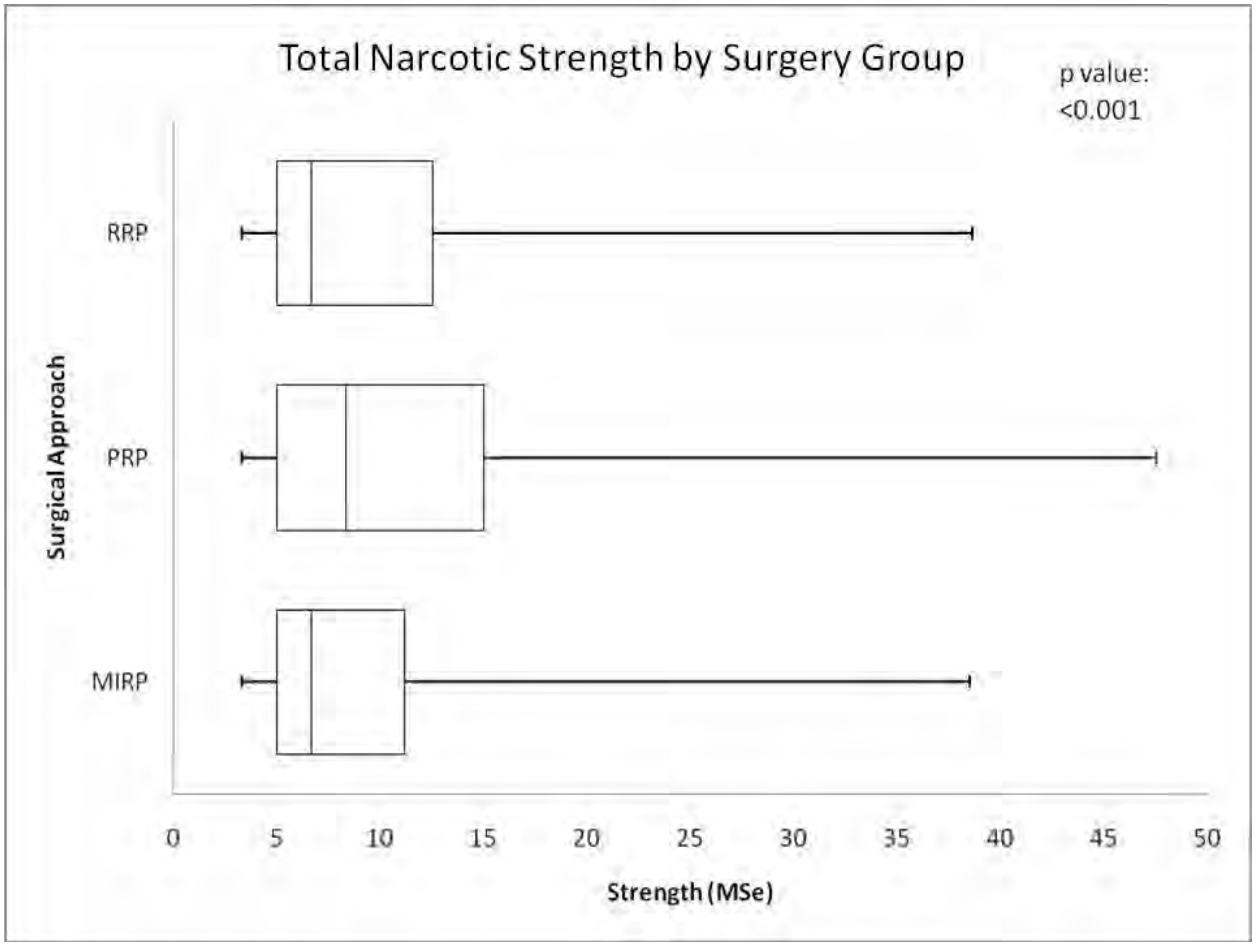

Table 1. Medicare payments within 6 months of radical prostatectomy by surgical approach.

	n	Mean	Median	p-value
All Medicare payments				
PRP	381	$11,953	$11,019	
MIRP	1548	$14,939	$13,335	p<0.001
RRP	5565	$14,301	$12,767	
Prostate cancer-related Medicare payments*				
PRP	381	$9,957	$9,339	
MIRP	1548	$12,289	$11,324	p<0.001
RRP	5565	$11,884	$10,853	

*Medicare Payments associated with ICD-9 185.0.

Table 2. Positive surgical margin percentile thresholds for surgeon volume of 5 to 12 radical prostatectomies based on binomial distribution and population means for pT2 and pT3a disease.

Surgeon Volume	Organ-confined disease, π = .0149		extracapsular extension, π =0.420	
N	n cases with positive margins (%)		n cases with positive margins (%)	
	25^{th} percentile	10^{th} percentile	25^{th} percentile	10^{th} percentile
5	2 (40)	3 (60)	4 (80)	5 (100)
6	2 (33)	3 (50)	4 (67)	5 (83)
7	3 (43)	3 (43)	5 (71)	6 (86)
8	3 (38)	4 (50)	5 (63)	6 (75)
9	3 (33)	4 (44)	6 (67)	7 (78)
10	3 (30)	4 (40)	6 (60)	7 (70)
11	3 (27)	4 (36)	7 (64)	8 (73)
12	4 (33)	5 (41)	7 (58)	8 (67)

Because of the discreteness of the binomial distribution, the cutoff rates are not identical for different surgeon volumes. Using the n's in this table, the 25^{th} and 10^{th} percentiles are actually (n-1)/N, but to reduce confusion, since correction action may be undertaken if surgeon-specific positive margin rates exceed the 25^{th}-percentiles, this table includes the minimum thresholds for the above percentiles.

Table 3. Adjusted model for predictors of surgical margin positivity.

Covariate (Referent)	Categories	OR (95% CI)	p-value
Age (≥75 years)	65-69	1.01 (0.69-1.46)	0.978
	70-74	1.03 (0.71-1.48)	0.877
Race (White)	Black	1.19 (0.84-1.69)	0.333
	Hispanic	0.91 (0.68-1.23)	0.547
	Asian	0.88 (0.58-1.34)	0.556
D'Amico Risk (Low)	Intermediate	2.52 (2.03-3.13)	<0.001
	High	3.68 (2.82-4.81)	<0.001
Surgical Approach (RRP)	MIRP	0.93 (0.77-1.13)	0.464
Surgeon Volume (Low)	Intermediate	1.0 (0.77-1.3)	0.989
	High	0.94 (0.74-1.18)	0.583
	Very High	1.02 (0.8-1.31)	0.845
SEER Region (San Fran.)	Detroit	1.16 (0.72-1.86)	0.534
	Iowa	1.41 (0.82-2.4)	0.213
	Seattle	1.43 (0.9-2.28)	0.125
	Utah	1.94 (1.17-3.22)	0.011
	Connecticut	1.23 (0.72-2.11)	0.451
	San Jose	1.24 (0.7-2.19)	0.460
	Los Angeles	1.56 (1.01-2.42)	0.047
	Greater California	1.17 (0.78-1.77)	0.440
	Kentucky	0.73 (0.42-1.26)	0.254
	Louisiana	0.68 (0.39-1.17)	0.160
	New Jersey	0.23 (0.12-0.43)	<0.001
	New Mexico/Georgia/Hawaii	0.54 (0.28-1.05)	0.071
Year (2004)	2005	0.83 (0.7-0.98)	0.033
	2006	0.75 (0.55-1.01)	0.057

Table 4. Adjusted model for predictors of secondary cancer treatment.

Covariate (Referent)	Categories	OR (95% CI)	p-value
Age (≥75 years)	65-69	1.11(0.8-1.54)	0.519
	70-74	0.94(0.67-1.31)	0.704
Race (White)	Black	1.08(0.77-1.53)	0.653
	Hispanic	0.81(0.59-1.12)	0.205
	Asian	1.3(0.91-1.86)	0.144
Marital Status (married)	Unmarried	0.94(0.74-1.19)	0.584
SEER Region (San Fran.)	20=Michigan	0.95(0.53-1.71)	0.859
	22=Iowa	1.97(1.14-3.4)	0.015
	25=Seattle	1.11(0.65-1.91)	0.704
	26=Utah	1.19(0.67-2.13)	0.553
	2=Connecticut	1.38(0.73-2.61)	0.320
	31=San Jose	1.79(0.97-3.32)	0.064
	35=Los Angeles	1.33(0.81-2.2)	0.260
	41=Greater California	1.6(1-2.54)	0.049
	42=Kentucky	1.53(0.88-2.66)	0.135
	43=Louisiana	1.4(0.81-2.4)	0.230
	44=New Jersey	1.67(0.97-2.89)	0.067
	New Mexico/Georgia/Hawaii	1.93(1.09-3.42)	0.023
D'Amico Risk (Low)	Intermediate	2.86(2.14-3.83)	<0.001
	High	8.3(6.13-11.22)	<0.001
Surgical Margin (Negative)	Positive	3.2(2.71-3.78)	<0.001
Surgical Approach (RRP)	MIRP	0.86(0.7-1.06)	0.151
Surgeon Volume (Low)	Intermediate	1.05(0.84-1.3)	0.683
	High	0.91(0.72-1.14)	0.405
	Very High	0.64(0.49-0.84)	0.001
Year (2004)	2005	0.98(0.82-1.16)	0.797
	2006	0.82(0.59-1.14)	0.236

Table 5. Cost Analysis of Adjuvant Cancer Treatments

	Radical Prostatectomy	Radical Prostatectomy and Hormonal Therapy	Radical Prostatectomy and Radiation	Radical Prostatectomy and Radiation with Hormonal Therapy	p-value
Baseline healthcare expenditures in the year prior to prostate cancer diagnosis, median	$1,861	$1,272	$1,380	$1,333	0.011
One year post-prostatectomy health care expenditures*, median	$15,022	$17,661	$28,442	$39,842	<0.001
Health care expenditures attributed to adjuvant therapies**	-	$1,367	$12,040	$23,487	<0.001

*We excluded men who underwent radical prostatectomy and adjuvant therapies more than 6 months after initial treatment (radical prostatectomy) to ensure that we fully captured the expense associated with primary and adjuvant therapy.

**One year pre-prostate cancer diagnosis expenditures and expenditures of radical prostatectomy alone, respectively subtracted from 12-month post-prostatectomy health care expenditures of various adjuvant therapies.

Table 6: Demographics of study population

		Percentage of patients in risk category			
	All patients (n=30,183)	Low (n=9,640)	Intermediate (n=12,966)	High (n=7,577)	P-value
Year					
2004	15784	53	52	52	0.30
2005	14399	47	48	48	
Age (years)					
65-69	9635	38	32	24	<0.001
70-74	8810	32	29	25	
≥ 75	11738	30	38	51	
Charlson score					
0	20246	69	68	64	<0.001
1	5940	20	19	20	
2+	2887	8	9	12	

Race*					
White	22796	77	76	73	<0.001
Black	3043	9	10	11	
Hispanic	1951	6	6	7	
Asian	1270	3	5	5	
Marital status**					
Not married	5978	18	19	23	<0.001
Married	20547	69	69	64	
% with high school education					
< 75	6970	22	23	25	<0.001
75-84.9	6585	21	22	23	
85-89.9	5617	18	19	18	
≥ 90	10991	38	37	33	
Household income ($)					
< 35,000	11454	35	38	42	<0.001
35,000 – 44,999	6927	23	23	23	

45,000 – 59,999	6426	23	21	19	
≥ 60,000	5356	19	18	15	
Population density					
Urban	27422	92	91	90	<0.001
Rural	2761	8	9	10	
Treatment					
Radical prostatectomy	5699	17	23	14	<0.001
ADT only	4441	7	13	27	
Cryotherapy	670	2	3	2	
Proton beam therapy	271	1	1	1	
Radiation therapies	15060	54	49	47	
Active surveillance	4042	19	12	9	
Pre-treatment imaging?	14443	36	49	61	<0.001

All percentages may not add to 100% due to rounding.

* Race was unknown/other in 1123 men; ** Marital status was unknown in 3658 men

Table 7: Multivariate analysis of demographic and clinical factors predictive of test utilization by risk category

	Low-risk (n=9,640)		Intermediate-risk (n=12,966)		High-risk (n=7,577)		All patients (n=30,183)	
	% use	OR	% use	OR	% use	OR	% use	OR
Age (years)								
65-69	34	REF	46	REF	63	REF	44	REF
70-74	37	0.99	53	1.11*	67	1.02	49	1.10*
≥ 75	36	1.12	49	1.14*	58	0.94	47	1.25*
Charlson score								
≥ 2	38	REF	51	REF	58	REF	47	REF
1	39	1.01	52	1.01	64	1	49	1.01
0	36	0.94	50	0.97	64	1.01	48	0.97
Race								
White	35	REF	49	REF	63	REF	47	REF
Black	38	1.03	51	1.15*	56	0.97	48	1.11*

Hispanic	36	1.05	47	0.95	58	0.98	45	0.98
Asian	36	0.92	49	0.94	64	0.85	49	0.95
Marital status								
Not married	37	REF	48	REF	59	REF	47	REF
Married	36	0.97	50	1.02	63	0.95	47	0.97
% with high school education								
< 75	37	REF	50	REF	57	REF	47	REF
75-84.9	38	0.93	51	0.95	61	0.99	48	0.96
85-89.9	37	0.89	50	0.90	63	0.98	48	0.93
≥ 90	33	0.77*	48	0.81*	63	0.90	45	0.84*
Household income ($)								
< 35,000	35	REF	48	REF	57	REF	45	REF
35,000 – 44,999	35	1.05	51	1.22*	63	1.14	48	1.11*
45,000 – 59,999	35	1.09	49	1.23*	64	1.20	46	1.09*
≥ 60,000	38	1.32*	51	1.32*	66	1.26*	48	1.19*

Population density								
Urban	35	REF	49	REF	61	REF	47	REF
Rural	37	1.26*	52	1.28*	58	1.11	48	1.22*
Treatment								
Radical prostatectomy	28	REF	41	REF	59	REF	40	REF
ADT only	32	0.99	41	0.88	44	0.62*	40	0.84*
Cryotherapy	37	1.44*	53	1.27*	74	1.64*	50	1.22*
Proton beam therapy	29	1.19	58	1.95*	80	2.14*	53	1.56*
Radiation therapies	46	1.82*	63	1.90*	79	2.21*	61	1.77*
Active surveillance	14	0.27	18	0.23*	21	0.16*	15	0.17*

* denotes significance at P<0.05 in multivariate logistic regression; OR = odds ratio

Table 8: Demographics of the study population from 2003-2006

	MIRP		RRP		p-value
	n	%	N	%	
Age					
<55	878	20.2	2833	18.3	
55-65	2440	56.1	8451	54.6	<0.0001
65-75	960	22.1	3796	24.5	
>75	72	1.7	391	2.5	
Region					
Northeast	391	9.0	1348	8.7	
Midwest	1623	37.3	4551	29.4	<0.0001
South	1507	34.6	5536	35.8	
West	800	18.4	3949	25.5	
missing	29	-	87	-	
Charlson Index					
0	1137	73.2	5897	72.7	
1-2	381	24.5	2049	25.3	0.80
≥3	35	2.3	169	2.1	
missing	2035	-	9952	-	

MIRP: minimally invasive radical prostatectomy; RRP: radical retropubic prostatectomy.

Table 9: Temporal trends in MIRP complications and iatrogenic injuries

	2003 (n=303)	2004 (n=743)	2005 (n=1044)	2006 (n=1644)	p-value
Mean LOS (days)	2.1	1.9	2.0	1.7	0.0044
Median LOS (days)	2.0	1.0	1.0	1.0	-
Heterologous transfusion	0.7	2.7	2.2	0.6	0.0047
Any complication within 30 days *	13.7	13.4	14.3	10.7	0.0218
Cardiac	1.7	1.0	0.7	0.7	0.0940
Respiratory	2.7	2.7	2.5	1.9	0.1660
Vascular/clot	0.3	0.8	1.5	1.5	0.0503
Wound/bleeding	1.4	0.8	1.1	1.1	0.9731
Genitourinary	3.1	4.7	3.9	2.5	0.0356
Miscellaneous medical	5.8	4.5	5.3	3.8	0.0991
Miscellaneous surgery	3.8	4.7	3.6	2.3	0.0046
Overall iatrogenic injuries within 30 days					
Intestinal injury	1.4	0.1	0.3	0.1	0.0492
Re-exploration	1.7	0.6	0.9	0.6	0.1935
Overall iatrogenic injuries within 6-12 months					
Rectal repair	1.4	1.5	1.3	0.4	0.16
Incisional hernia repair	1.2	2.0	1.7	-	0.7408
Stricture	6.4	6.9	5.7	6.1	0.6033

All values in percentages unless otherwise stated; MIRP: minimally invasive prostatectomy; LOS: length of stay. Trend for mean LOS assessed with GLM, all other p-values are two-sided Cochran-Armitage Tests for Trend.

*If patients had more than one complication type then this was counted as one complication.

Table 10: Temporal trends in RRP complications and iatrogenic injuries

	2003 (n=4686)	2004 (n=4243)	2005 (n=3587)	2006 (n=2955)	p-value
Mean LOS (days)	3.2	3.1	3.1	2.9	0.0001
Median LOS (days)	3.0	3.0	3.0	3.0	-
Heterologous transfusion	9.1	9.3	9.4	6.6	<0.001
Any complication within 30 days *	18.1	17.1	18.4	14.8	0.0072
Cardiac	2.1	1.5	1.8	1.4	0.0664
Respiratory	4.3	4.7	5.0	3.8	0.6257
Vascular/clot	2.3	1.9	2.1	2.1	0.7069
Wound/bleeding	2.1	1.5	1.5	1.2	0.0034
Genitourinary	2.3	2.7	2.8	2.6	0.3823
Miscellaneous medical	5.9	5.8	6.5	5.0	0.3955
Miscellaneous surgery	4.6	4.1	4.3	3.4	0.0325
Overall iatrogenic injuries within 30 days					
Intestinal injury	0.4	0.6	0.3	0.5	0.6231
Re-exploration	0.1	0.1	0.2	0.	0.7409
Overall iatrogenic injuries within 6-12 months					
Rectal repair	1.1	1.2	1.2	0.8	0.5851
Incisional hernia repair	0.9	0.8	1.3	-	0.1597
Stricture	13.1	13.1	12.6	12.0	0.2372

All values in percentages unless otherwise stated; RRP: radical retropubic prostatectomy; LOS: length of stay

*If patients had more than one complication type then this was counted as one complication.

Table 11: Comparison of overall complications and overall iatrogenic injury rates between RRP and MIRP

	MIRP (n=4350)		RRP (n=15471)		p-value
	n	%	n	%	
Mean LOS (days)	1.9		3.1		<0.0001
Median LOS (days)	1		3		-
Heterologous transfusion	63	1.5	1351	8.7	<0.0001
Any complication within 30 days *	507	12.5	2492	17.3	<0.0001
Cardiac	33	0.8	249	1.7	<0.0001
Respiratory	93	2.3	649	4.5	<0.0001
Vascular/clot	53	1.3	298	2.1	0.0018
Wound/bleeding	42	1.0	229	1.6	0.0099
Genitourinary	136	3.4	375	2.6	0.0095
Miscellaneous medical	183	4.5	845	5.9	0.0010
Miscellaneous surgery	131	3.2	597	4.1	0.0088
All iatrogenic injuries within 30 days					
Intestinal injury	11	0.3	62	0.4	0.1555
Re-exploration	231	0.8	17	0.1	<0.0001
All iatrogenic injuries within 6-12 months					
Rectal repair	31	1.1	134	1.0	0.8486
Incisional hernia repair	31	1.8	92	1.0	0.0054
Stricture	180	6.2	1553	12.8	<0.0001
Cystography within 30 days	1439	35.5	1307	9.1	<0.0001

All values in percentages unless otherwise stated; RRP: radical retropubic prostatectomy; MIRP: minimally invasive radical prostatectomy; LOS: length of stay

*If patients had more than one complication type then this was counted as one complication.

Table 12. Baseline Patient Demographics

	MIRP n = 2206	PRP n = 463	RRP n = 8037	p value
Preoperative Narcotic Use	260 (11.8)	70 (15.1)	1093 (13.6)	0.146
Age				
<55	547 (24.8)	105 (22.7)	1807 (22.5)	0.002
55-64	1213 (55.0)	247 (53.4)	4272 (53.2)	
65-74	422 (19.1)	109 (23.5)	1866 (23.2)	
>75	24 (1.1)	2 (0.4)	92 (1.1)	
Insurance				
Comprehensive	622 (28.2)	155 (33.5)	2095 (26.1)	<0.001
HMO	313 (14.2)	66 (14.3)	1606 (20.0)	
PPO	962 (43.6)	192 (41.5)	3325 (41.4)	
POS	277 (12.6)	41 (8.9)	896 (11.2)	
Other	12 (0.5)	1 (0.2)	24 (0.3)	
Unknown	20 (0.9)	8 (1.7)	91 (1.1)	
Charlson Comorbidity Index				
0	1661 (75.3)	336 (72.6)	6317 (78.6)	0.005
1	330 (15.0)	87 (18.8)	1304 (16.2)	
2	42 (1.9)	13 (2.8)	169 (2.1)	
3+	28 (1.3)	4 (0.9)	50 (0.6)	
Unknown	145 (6.6)	23 (5.0)	197 (2.5)	
Geography				
Midwest	914 (41.4)	177 (38.2)	2565 (31.9)	<0.001
Northeast	203 (9.2)	17 (3.7)	650 (8.1)	
South	730 (33.1)	213 (46.0)	2829 (35.2)	
West	350 (15.9)	51 (11.0)	1948 (24.2)	
Unknown	9 (0.4)	5 (1.1)	45 (0.6)	

Table 13. Postoperative narcotic prescription refills by surgical approach

	MIRP n (%)	PRP n (%)	RRP n (%)	Overall n (%)	p value
Additional Refills Required*	445 (20.2)	196 (42.3)	2319 (28.9)	2960 (27.6)	<0.001
Number of Additional Refills					
1	265 (12.0)	114 (24.6)	1498 (18.6)	1877 (17.5)	<0.001
2	89 (4.0)	45 (9.7)	354 (4.4)	488 (4.6)	
≥3	91 (4.1)	37 (8.0)	467 (5.8)	595 (5.6)	

*After filling initial postoperative prescription

Table 14. Multivariate model of total postoperative narcotic prescription strength (in MSe), narcotic prescription refills needed, and total postoperative narcotic cost.

	Total Strength			Additional Refills			Total Cost		
	RR	95% CI	p value	OR	95% CI	p value	RR	CI	p valu
Surgical Approach (vs. RRP)									
MIRP	0.97	(0.93-1.01)	0.104	0.61	(0.54-0.69)	<0.001	0.94	(0.90-0.98)	0.00
PRP	1.11	(1.03-1.21)	0.010	1.75	(1.43-2.15)	<0.001	1.16	(1.08-1.26)	<0.0(
Age (vs. >75y)									
<55	1.22	(1.04-1.43)	0.015	2.22	(1.38-3.59)	0.001	1.48	(1.26-1.73)	<0.0(
55-64	1.17	(1.01-1.37)	0.045	1.66	(1.04-2.67)	0.035	1.34	(1.15-1.57)	<0.0(
65-74	1.13	(0.97-1.32)	0.126	1.27	(0.79-2.05)	0.326	1.17	(1.01-1.37)	0.04
Region (vs. West)									
South	1.18	(1.12-1.24)	<0.001	1.07	(0.93-1.22)	0.329	0.91	(0.87-0.95)	<0.0(
Midwest	0.84	(0.79-0.91)	<0.001	0.78	(0.64-0.96)	0.016	0.78	(0.73-0.84)	<0.0(
Northeast	1.01	(0.96-1.06)	0.674	1.14	(1.00-1.30)	0.050	1.14	(1.09-1.19)	<0.0(
Insurance plan (vs. HMO)									
Comprehensive	1.02	(0.97-1.08)	0.404	0.94	(0.81-1.10)	0.428	1.01	(0.96-1.07)	0.59
PPO	0.95	(0.91-1.00)	0.045	0.82	(0.72-0.93)	0.002	0.92	(0.88-0.97)	<0.0(
POS	0.94	(0.88-1.00)	0.064	0.79	(0.66-0.94)	0.009	1.00	(0.94-1.07)	0.99
Other	0.89	(0.67-1.20)	0.449	0.99	(0.46-2.13)	0.980	0.62	(0.46-0.83)	<0.0(
Baseline Narcotic Use (vs. None)	2.70	(2.56-2.84)	<0.001	2.85	(2.50-3.25)	<0.001	3.00	(2.85-3.15)	<0.0(
Charlson score (vs. ≥3)									
0	0.99	(0.82-1.19)	0.904	0.80	(0.49-1.30)	0.370	0.90	(0.75-1.08)	0.24
1	1.18	(0.98-1.42)	0.084	1.06	(0.64-1.75)	0.820	1.09	(0.91-1.31)	0.32
2	1.13	(0.92-1.40)	0.252	0.90	(0.51-1.59)	0.716	0.95	(0.77-1.17)	0.61

Appendix. Morphine Sulfate Equivilants conversion table (MSe)

Active Ingredient	Mg Dose eq to 1 MSe*	Dosing Schedule
Codeine	4.33	3 to 4 hours
Hydrocodone	1	3 to 4 hours
Hydromorphone	0.25	3 to 4 hours
Meperidine	10	2 to 3 hours
Morphine	2	3 to 4 hours
MS Contin	1	3 to 4 hours
Oxycodone	1	3 to 4 hours
Oxycontin	1	3 to 4 hours
Pentazocine	5	3 to 4 hours
Propoxyphene	4.33	4 to 6 hours
Tramadol	3.33	6 hours

*1 Mse equals 10 mg meperidine or 1 mg morphine sulfate

PUBLICATIONS DURING REPORTING PERIOD

Comparative Effectiveness of Perineal Versus Retropubic and Minimally Invasive Radical Prostatectomy

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Purpose: While perineal radical prostatectomy has been largely supplanted by retropubic and minimally invasive radical prostatectomy, it was the predominant surgical approach for prostate cancer for many years. In our population based study we compared the use and outcomes of perineal radical prostatectomy vs retropubic and minimally invasive radical prostatectomy.

Materials and Methods: We identified men diagnosed with prostate cancer from 2003 to 2005 who underwent perineal (452), minimally invasive (1,938) and retropubic (6,899) radical prostatectomy using Surveillance, Epidemiology and End Results-Medicare linked data through 2007. We compared postoperative 30-day and anastomotic stricture complications, incontinence and erectile dysfunction, and cancer therapy (hormonal therapy and/or radiotherapy).

Results: Perineal radical prostatectomy comprised 4.9% of radical prostatectomies during our study period and use decreased with time. On propensity score adjusted analysis men who underwent perineal vs retropubic radical prostatectomy had shorter hospitalization (median 2 vs 3 days, $p < 0.001$), received fewer heterologous transfusions (7.2% vs 20.8%, $p < 0.001$) and required less additional cancer therapy (4.9% vs 6.9%, $p = 0.020$). When comparing perineal vs minimally invasive radical prostatectomy men who underwent the former required more heterologous transfusions (7.2% vs 2.7%, $p = 0.018$) but experienced fewer miscellaneous medical complications (5.3% vs 10.0%, $p = 0.045$) and erectile dysfunction procedures (1.4 vs 2.3/100 person-years, $p = 0.008$). The mean and median expenditure for perineal radical prostatectomy in the first 6 months postoperatively was $1,500 less than for retropubic or minimally invasive radical prostatectomy ($p < 0.001$).

Conclusions: Men who undergo perineal vs retropubic and minimally invasive radical prostatectomy experienced favorable outcomes associated with lower expenditure. Urologists may be abandoning an underused but cost-effective surgical approach that compares favorably with its successors.

Key Words: prostate, prostatic neoplasms, prostatectomy, perineum, complications

Abbreviations and Acronyms

ED = erectile dysfunction

MIRP = minimally invasive RP

PLND = pelvic lymph node dissection

PRP = perineal RP

RP = radical prostatectomy

RRP = retropubic RP

SEER = Surveillance, Epidemiology and End Results

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Study received institutional review board approval.

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After the first reported series of RP via a perineal approach in 1905, PRP became the standard prostate cancer surgical treatment for much of the 20th century.[1] Perineal incision proximity to the prostate, decreased blood loss, minimal pain, and ease of the approach in obese men and in those with prior abdominal surgery contributed to PRP being the predominant approach. PRP use decreased after the popularity of external beam radiation therapy in the 1970s and the description of nerve sparing RRP by

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Walsh et al in the 1980s, which obviated the need for a second incision for PLND.[2] However, after the advent of prostate specific antigen screening, resultant stage migration and increasing adoption of MIRP, the PLND rate during RP decreased.[3] Also, the indication for and benefit of PLND has been debated for low risk disease.[4] Given that PRP is associated with less postoperative pain and a shorter hospital stay than RRP, it was suggested that PRP may be underused in cases in which concurrent PLND is unnecessary.[5,6]

In the absence of randomized, controlled trials, population based studies of comparative effectiveness allow the evaluation of competing therapies across a broad range of providers in various health settings. We determined contemporary PRP use and outcomes compared to those of MIRP and RRP.

MATERIALS AND METHODS

Data

Our study was approved by the institutional review board. Participants were de-identified and the consent process was waived. We identified 137,217 men 65 years old or older who were diagnosed with prostate cancer from 2002 to 2005 and followed through December 31, 2007 using SEER-Medicare linked data.[7]

Study Exclusions

Excluded from analysis were 10,441 men enrolled in a health maintenance organization and/or those not enrolled in Medicare Parts A and B throughout the study duration since claims are not reliably submitted in these men. To increase sensitivity to detect postoperative radiation therapy we restricted analysis to men with prostate cancer diagnosed as the only cancer and excluded 4,628 with other cancers. This yielded a study cohort of 9,289 men who underwent RP during 2003 to 2007 based on CPT-4 codes, including 55840, 55842 and 55845 for RRP, 55866 for MIRP, and 55810, 55812 and 55815 for PRP. Other groups have used CPT-4 code 55899 (unspecified male genitourinary procedure) with a RRP CPT-4 code to ascertain MIRP but Medicare does not recognize this coding variant and it was excluded from analysis.

Outcomes

We examined mortality/morbidity, length of stay, anastomotic stricture, incontinence and ED diagnoses and procedures, and additional cancer therapy. Postoperative complications by category and transfusions were assessed within 30 days of surgery. Postoperative mortality was defined as death within 30 days of RP. We assessed anastomotic strictures 31 to 365 days after surgery. Incontinence and ED diagnoses and procedures were evaluated more than 18 months after surgery, which is the time required for urinary and sexual function recovery to plateau.[8] Finally, we identified men who underwent additional cancer therapy (radiation and/or hormonal treatment) after prostatectomy as a surrogate for cancer control.[9]

Expenditures

To best attribute the costs associated with competing surgical approaches we assessed Medicare payments for 6 months including and after RP as 1) total Medicare reimbursements and 2) prostate cancer related Medicare reimbursements for claims submitted with a prostate cancer diagnosis code (ICD-9 185.0).

Control Variables

Patient age was obtained from the Medicare file. The SEER registry provided data on race/ethnicity, census measurements of median household income and the proportion of individuals with at least a high school education, SEER region, population density and marital status. Due to small numbers we combined the New Mexico, rural Georgia and Atlanta SEER registries. Comorbidity using the Klabunde modification of the Charlson index, and preoperative diagnoses of incontinence and ED were based on inpatient, outpatient and carrier claims during the year before surgery.[10] Finally, we adjusted for year of surgery since outcomes may have improved with time.

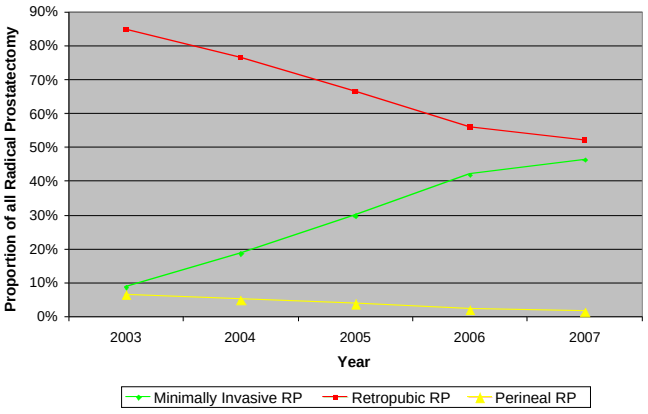
Statistical Analysis

PRP, RRP and MIRP annual use rates were derived and temporal trends in use were compared with the Mantel-Haenszel chi-square test for trend, adjusted for surgeon clustering. For dichotomous outcomes occurring within a fixed interval, such as 30 and 31 to 365-day (anastomotic stricture) outcomes, we compared proportions (the number of events divided by the number of patients) for PRP vs MIRP and RRP. We compared rates for outcome variables without an upper time bound for which followup could vary.[11] We also compared median length of stay among the groups.

Since men who underwent PRP differed from those who underwent MIRP and RRP in terms of demographic characteristics, we used weighted propensity score methods to adjust for these differences.[12,13] Propensity score methods control for all observed confounding factors that may influence group assignment and outcome using a single composite measure. They also balance patient characteristics between groups, as would occur in a randomized experiment.

To perform propensity score adjustment we used a logistic regression model to calculate the probability of undergoing PRP vs MIRP and RRP based on all covariates described, and then weighted data on each patient based on the inverse propensity of being in 1 of the 2 treatment groups.[14] Covariate balance was assessed after adjustment. We used generalized estimating equations to account for surgeon clustering on weighted propensity adjusted analysis. To compare proportions we fit generalized estimating equation logistic regressions with surgical approach (PRP vs MIRP and RRP) as the only covariate, weighted by the inverse propensity score. All tests were considered statistically significant at $\alpha = 0.05$. All analysis was done with SAS®, version 9.1.3.

Due to confidentiality, values less than 11 may not be reported directly or in a derivable way for any SEER-Medicare data obtained from the National Cancer Institute. Therefore, for any patient group with fewer than 11 patients, data are shown as less than 2.4% in the PRP



RP rate by approach during study period

group, less than 0.6% in the MIRP group and less than 0.2% in the RRP group.

RESULTS

From 2003 to 2007 in the study cohort 6,899 men underwent RRP, 1,938 underwent MIRP and 452 underwent PRP. During the study period we found increased use of MIRP with a corresponding decrease in the rate of RRP and PRP (see figure). PRP use decreased more than 3-fold during the study period. Less than 2% of RPs were done via a perineal approach in 2007 vs 6.5% in 2003.

We noted multiple demographic differences in PRP vs MIRP and RRP. Men undergoing PRP vs MIRP were more likely to have comorbidities ($p = 0.008$). Men with lower education and median income were more likely to undergo PRP than MIRP ($p = 0.028$ and <0.001, respectively). Men undergoing PRP vs MIRP were more likely to reside in a nonmetropolitan area ($p < 0.001$). PRP was more commonly done in the South and Midwest compared to MIRP and RRP ($p = 0.014$ and 0.004, respectively). Baseline incontinence was lower for PRP vs MIRP and RRP ($p < 0.001$ and 0.040, respectively). While baseline ED was lower for PRP vs MIRP ($p < 0.001$), there were no differences compared to RRP. We also noted no differences in age, race, marital status, or tumor grade or stage by surgical approach.

When comparing unadjusted outcomes, men undergoing PRP vs RRP had shorter length of stay (2 vs 3 days, $p < 0.001$), and were less likely to undergo blood transfusion (7.1% vs 20.1%, $p < 0.001$) and have anastomotic stricture (8.2% vs 14.2%, $p = 0.002$). The overall 30-day complication rate was lower in men undergoing PRP vs RRP (16.7% vs 23.4%, $p = 0.002$). However, additional cancer therapy did not differ for PRP vs RRP (5.8% vs 6.9%, $p = 0.147$). When we compared unadjusted outcomes in the PRP and MIRP cohorts, men undergoing PRP vs MIRP were more likely to undergo blood transfusion (7.1% vs 2.5%, $p < 0.001$). However, the 30-day complication rate was higher in the MIRP group (16.7% vs 21.9%, $p = 0.016$) while anastomotic stricture rate was higher in the PRP cohort (8.2% vs 5.3%, $p = 0.048$). Finally, PRP had the lowest mean and median Medicare expenditures, followed by RRP and MIRP (see table).

On propensity score adjusted analysis PRP vs RRP was associated with fewer blood transfusions (7.2% vs 20.8%, $p < 0.001$) and shorter length of stay (median 2 vs 3 days, $p < 0.001$). The additional cancer therapy incidence (radiation and hormonal) was higher in the RRP group (4.9% vs 6.9%, $p = 0.020$). There were no differences in PRP vs RRP 30-day complications, mortality, postoperative stricture, or ED or incontinence diagnosis and treatment. When comparing outcomes between PRP and MIRP, PRP was associated with more blood transfusions (7.2% vs 2.7%, $p = 0.018$), fewer miscellaneous medical complications (5.3% vs 10.0%, $p = 0.045$) and fewer procedures for ED (1.4 vs 2.3/100 person-years, $p = 0.008$). MIRP and PRP did not differ in length of stay, overall 30-day complications, mortality, incontinence diagnosis or procedures and additional cancer therapy.

DISCUSSION

RP gained popularity through the mid 1900s with a demonstrated survival benefit for prostate cancer.[15] In the 1970s an evolution from the perineal to the retropubic approach occurred due to the loss of familiarity with perineal surgical anatomy as simple open perineal prostatectomy was abandoned, familiarity with retropubic anatomy as simple retropubic open prostatectomy and radical cystectomy became more common, and increased interest in PLND and the lack of the need for a second incision to perform lymphadenectomy (P. Walsh, personal communication, November 16, 2009). However, with the subse-

Medicare payments within 6 months of RP by surgical approach

	No. Pts	Mean/Median Payment* ($)
Overall:		
PRP	381	11,953/11,019
MIRP	1,548	14,939/13,335
RRP	5,565	14,301/12,767
Prostate Ca (ICD-9 185.0):		
PRP	381	9,957/9,339
MIRP	1,548	12,289/11,324
RRP	5,565	11,884/10,853

* $p < 0.001$.

quent use of prostate specific antigen for prostate cancer screening in the 1990s and corresponding stage migration, the incidence of positive lymph nodes at RP has decreased to less than 3%.[16] Given the low rate of lymph node involvement, the need for concurrent PLND during RP remains debatable. Also, prior groups noted that PRP has shorter operative time and decreased intraoperative operative cost than MIRP or RRP,[17] although the increased surgical expense may be offset by significantly lower nonoperative hospital costs. This was the finding in a retrospective review of 452 patients treated for clinically localized prostate cancer in which total hospital cost differences were less for minimally invasive approaches (robot assisted MIRP and cryosurgical ablation of the prostate) than in the open (PRP or RRP) surgery groups.[18] However, these studies did not account for delayed costs, such as treatment for ED or urinary incontinence, salvage therapy and associated time lost at work. Additional analysis is needed to completely capture these associated costs.

We performed a population based analysis comparing PRP vs RRP and MIRP outcomes with several important findings. 1) We found a significant increase in the rate of MIRP use with concomitant cannibalization of RRP and PRP. During the study period PRP decreased from 6.5% to less than 2% of all RPs done in this cohort. As the scientific literature balances reports of costs and mixed outcomes of MIRP,[17–20] competing approaches to RP may come under greater scrutiny by payors, patients and physicians. This decreased use limits PRP training and exposure of this approach to the next generation of urologists. A survey of recent urology residents revealed that only 13% of those not exposed to PRP used the procedure in practice.[20]

2) Men undergoing MIRP vs PRP were more likely to come from areas of higher socioeconomic status and from metropolitan areas. This difference may be due to the successful marketing approach of robot-assisted MIRP through print media and the Internet as well as early adoption of the robot at wealthier centers.[11]

3) When we compared men undergoing PRP vs RRP, PRP was associated with shorter length of stay and fewer heterologous blood transfusions. While there was no difference in the postoperative stricture rate between PRP and RRP, PRP was associated with less adjuvant therapy use. While this may reflect improved cancer control after PRP, it may also reflect differences in lymph node sampling since adjuvant therapy may be initiated with node positive disease that remains undiagnosed by PRP alone. PRP was associated with lower cost due to decreased median hospital stay, blood transfusion and adjuvant therapy use, consistent with a single institution comparison.[18] Also, total Medicare payments within 6 months of surgery were lower for PRP than for RRP or MIRP with a mean and median PRP expenditure greater than $1,500 less than that for RRP or MIRP. While this may not capture all payments associated with long-term complications beyond 6 months postoperatively, it captures the associated expense of rehospitalizations, emergency department visits and additional radiological or surgical procedures.

4) Comparison between men undergoing PRP vs MIRP revealed no difference in length of stay, although PRP was associated with a 3-fold increase in the likelihood of heterologous blood transfusion. However, this increased PRP blood transfusion rate was not offset by any MIRP advantages in short-term or intermediate term outcomes. MIRP was associated with an almost 2-fold higher rate of medical complications within 30 days of surgery compared with PRP. Cancer control and stricture rates did not differ significantly for PRP vs MIRP.

5) PRP vs MIRP was associated with fewer procedures for ED but we did not account for surgeon skill and experience. For instance, PRP surgeons who have not changed to newer approaches may be comfortable with their PRP ability due to greater experience and proficiency, resulting in better outcomes.

Our findings must be interpreted in the context of the study design. 1) Our study was restricted to Medicare beneficiaries older than 65 years who resided in SEER regions. Thus, these results may not be applicable to younger men or those undergoing surgery outside SEER regions due to geographic variation in RP use and outcomes.[21] 2) We could not distinguish between MIRP with and without robotic assistance since the 2 procedures share a common CPT-4 code. However, robotic assisted MIRP use surged from 1% of RPs in 2001 to 40% in 2006,[22,23] with a current estimate of 50% to 70%.[24] Concurrently MIRP without robotic assistance is disappearing in the United States, consistent with a recent survey of urologists showing a 25% to 75% decrease in surgical volume among those using a nonrobotic approach to RP.[25,26] 3) Observer bias may have a role in the diagnosis of ED and urinary continence, as captured by Medicare claims data. Men diagnosed with these conditions were sufficiently bothered to bring it to the attention of physicians who entered the diagnosis. Patient self-report using validated quality of life instruments remains the gold standard to assess these outcomes. 4) As in any adjusted analysis, propensity score methods cannot control for unmeasured confounders and have other limitations.[27]

CONCLUSIONS

Despite decreased use, PRP has outcomes that are equivalent or improved compared to those of RRP and MIRP with lower cost within the first 6 months postoperatively. Since there is increased attention on comparative effectiveness analysis due to increasing health care costs, our findings contribute to other studies showing that PRP is a favorable and perhaps prematurely abandoned alternative to RP.

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Original Article

Utilization and Expense of Adjuvant Cancer Therapies Following Radical Prostatectomy

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BACKGROUND: We sought to identify the costs of adjuvant therapies following radical prostatectomy (RP) and factors associated with their receipt. **METHODS:** We used SEER-Medicare data from 2004-2006 to identify 4247 men who underwent RP, of whom 600 subsequently received adjuvant therapies. We used Cox regression to identify factors associated with receipt of adjuvant therapies. Health care expenditures within 12 months of diagnosis were compared for RP alone versus RP with adjuvant therapies. **RESULTS:** Biopsy Gleason score, prostate-specific antigen, risk group, and SEER region were significantly associated with receipt of adjuvant treatments (all $P<.001$). Higher surgeon volume was associated with lower odds of receiving adjuvant therapies (hazard ratio [HR], 0.60; 95% confidence interval [CI], 0.46-0.78 [$P<.001$]). Factors associated with increased receipt of adjuvant therapies were positive surgical margins (HR, 3.02; 95% CI, 2.55-3.57 [$P<.001$]), high-risk group versus low-risk group (HR, 7.65; 95% CI, 5.64-10.37 [$P<.001$]), lymph node–positive disease (HR, 5.36; 95% CI, 3.71-7.75 [$P<.001$]), and treatment in Iowa (HR, 1.93; 95% CI, 1.12-3.32 [$P = .019$]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95% CI, 1.09-3.39 [$P = .025$]) versus San Francisco SEER regions (baseline). Age, race, comorbidities, and surgical approach were not associated with use of adjuvant therapies. The median expenditures attributable to postprostatectomy hormonal therapy, radiation therapy, and radiation with hormonal therapy versus were $1361, $12,040, and $23,487. **CONCLUSIONS:** Men treated by high-volume surgeons were less likely to receive adjuvant therapies. Regional variation and high-risk disease characteristics were associated with increased receipt of adjuvant therapies, which increased health care expenditures by 2- to 3-fold when radiotherapy was administered. ***Cancer* 2011;00:000–000.** © *2011 American Cancer Society*.

KEYWORDS: prostatectomy, adjuvant therapy, utilization, expenditures, outcomes.

Prostate cancer remains the most commonly diagnosed solid organ tumor among men in the United States, with approximately 192,000 incident cases in 2009.[1] The majority of these tumors are localized, and radical prostatectomy (RP) remains the most popular treatment option.[2] However, 21%-37% of men experience biochemical recurrence (BCR) after radical prostatectomy.[3] Recent studies have shown that postprostatectomy radiotherapy improves prostate cancer–specific survival[4] and significantly decreases overall mortality when used in the adjuvant[5] or salvage setting in selected men with high-risk disease.[6] Furthermore, the benefit of hormonal therapy needs to be carefully balanced against the significant inherent risks of cardiovascular and thromboembolic disease, along with the substantial health care costs of implementing this treatment.[7-9] Hormonal therapy as it pertains to the adjuvant setting, either alone or in combination with radiotherapy, has been less extensively evaluated, with no definitive guidelines on who should receive treatment or when to initiate it.[8,9]

Although there are few contemporary characterizations of secondary therapies,[6,10,11] a study of Medicare beneficiaries from the early 1990s demonstrated that 35% of men receive secondary therapies following RP.[12] However, this may not reflect contemporary practice patterns due to the downward stage migration that followed the advent of prostate-specific antigen (PSA) screening.[13] The purpose of our population-based study was to evaluate factors associated with the use of adjuvant cancer therapies following RP and estimate the associated health care expenditures of these treatments.

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MATERIALS AND METHODS

The study was approved by the Brigham and Women's Institutional Review Board. Patient data were de-identified and the requirement for consent was waived. We used Surveillance, Epidemiology, and End Results (SEER)-Medicare data for analysis, which comprise a linkage of population-based cancer registry data from 16 SEER areas with Medicare administrative data and cover approximately 26% of the United States population. The Medicare program provides benefits to 97% of Americans aged $\geq$65 years.[14]

Study Cohort

We identified 4247 men aged $\geq$65 years who were diagnosed with prostate cancer in 2004 and 2005 and underwent RP through 2006 based on the Physician's Current Procedural Terminology Coding System, 4th edition, (CPT-4): codes 55840, 55842, 55845 for open RP and code 55866 for minimally invasive RP. CPT-4 code 55899 (unspecified male genitourinary procedure) may sometimes be used with an open RP administrative code to specify minimally invasive RP with robotic assistance for private health plans,[15] but Medicare does not recognize this coding schema, and very few men had this combination of codes; therefore, this schema was not used to identify minimally invasive RP. We excluded men not enrolled in both Medicare Part A and B, or who were enrolled in a Medicare health maintenance organization (because their claims are not reliably submitted). Because SEER only captures positive margin characteristics for American Joint Commission on Cancer pathological T2 and T3a disease, we excluded 292 men with pathological stage T3b, 63 men with pathological stage T4, and 412 men with missing margin status from our cohort. Patients with lymph node–positive disease (n = 45) were included in the study. In addition, to increase the sensitivity for detecting additional postoperative radiation therapy, we restricted our cohort to patients with prostate cancer diagnosed as their only cancer. A total of 204 patients with other cancers, including nonmelanoma skin cancers, were excluded from the analysis.

Outcomes

We examined the utilization of adjuvant therapy (radiation and/or hormonal) after RP in patients with pathological T2 and T3a disease.[12,16] According to the American Urological Association 2007 guidelines, additional radiation and/or hormonal therapy should be administered to patients with adverse pathological features and/or positive surgical margins.[17]

Control Variables

Age was obtained from each patient's Medicare file; race, census tract measures of median household income and high school education, region, population density (urban vs rural), and marital status were obtained from SEER registry data. Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery.[18] The Klabunde modification uses comorbid conditions identified by the Charlson comorbidity index and incorporates the diagnostic and procedure data contained in Medicare physician (Part B) claims. Variables were categorized as in Table 1. Additionally, we used PSA, Gleason grade, and clinical stage to stratify men to low, intermediate, and high-risk disease.[19] However, tumor stage was missing/unknown for almost one-third of our patients, and we therefore used a modified risk stratification without clinical stage, resulting in a low-risk designation for 29% of our cohort. Therefore, we used a modified risk classification defined as follows: PSA $<$10 and biopsy Gleason score $<$7 = low; PSA 10-20 or Gleason score 7 = intermediate; PSA $>$20 or Gleason score $>$7 = high.

Because surgeon rather than hospital volume is the more significant determinant of outcomes following open RP,[20] we determined surgeon volume for each type of procedure by aggregating the number of procedures performed from 2004-2006. Surgeon volume was categorized into quartiles, consistent with a prior study.[21]

Expenditures Related to the Use of Adjuvant Cancer Therapies

We compared baseline health care expenditures in the 12 months prior to prostate cancer diagnosis for men who underwent RP alone versus those who underwent adjuvant treatment postprostatectomy. To determine the total expense of adjuvant treatment, we summed the total health care expenditures from the beneficiary, Medicare, and supplemental private insurance for inpatient, outpatient, and physician services within 12 months of prostate cancer diagnosis. Approximately 50% of men who received adjuvant therapies did so within 6 months, and we were able to capture costs for 275 of the 600 that received therapy. To ensure that we adequately captured the cost of treatment, we excluded men who underwent RP and adjuvant therapies beyond 6 months following prostate cancer

Table 1. Demographics of the Study Population

Characteristic	Categories	Total	No Adjuvant Therapy	Hormonal or Radiation	*P*	Hormonal Therapy	Radiation Therapy
Year of surgery	2004	1779	1503 (84.49)	275 (15.46)	.028	138 (7.76)	221 (12.42)
	2005	2058	1776 (86.30)	282 (13.70)		139 (6.75)	214 (10.40)
	2006	410	367 (89.51)	43 (10.49)		17 (4.15)	39 (9.51)
Age (years)	65-69	2620	2240 (85.50)	379 (14.47)	.624	177 (6.76)	310 (11.83)
	70-74	1332	1154 (86.64)	178 (13.36)		95 (7.13)	137 (10.29)
	≥75	295	252 (85.42)	43 (14.58)		22 (7.46)	27 (9.15)
Charlson comorbidity index	0	2956	2543 (86.03)	413 (13.97)	.501	194 (6.56)	343 (11.60)
	1	1018	865 (84.97)	153 (15.03)		85 (8.35)	106 (10.41)
	≥2	273	238 (87.18)	34 (12.45)		15 (5.49)	25 (9.16)
Race	White	3366	2893 (85.95)	473 (14.05)	.328	226 (6.71)	384 (11.41)
	Black	307	265 (86.32)	42 (13.68)		22 (7.17)	31 (10.10)
	Hispanic	356	310 (87.08)	45 (12.64)		25 (7.02)	30 (8.43)
	Asian	186	150 (80.65)	36 (19.35)		20 (10.75)	25 (13.44)
	Other	32	28 (87.50)	4 (12.50)		1 (3.13)	4 (12.50)
Marital status	Unmarried	605	523 (86.45)	82 (13.55)	.632	35 (5.79)	67 (11.07)
	Married	3469	2971 (85.64)	497 (14.33)		247 (7.12)	393 (11.33)
Education: % of census tract with at least a high school degree	<75	785	672 (85.61)	112 (14.27)	.074	57 (7.26)	83 (10.57)
	75-84.99	785	682 (86.88)	103 (13.12)		60 (7.64)	76 (9.68)
	85-89.99	791	656 (82.93)	135 (17.07)		63 (7.96)	113 (14.29)
	≥90	1885	1635 (86.74)	250 (13.26)		114 (6.05)	202 (10.72)
Median income in census tract of residence	<$35,000	1106	938 (84.81)	168 (15.19)	.367	88 (7.96)	124 (11.21)
	$35,000-44,000	975	842 (86.36)	132 (13.54)		64 (6.56)	102 (10.46)
	$45,000-59,000	1072	912 (85.07)	160 (14.93)		76 (7.09)	134 (12.50)
	≥$60,000	1093	953 (87.19)	140 (12.81)		66 (6.04)	114 (10.43)
SEER region	San Francisco	171	151 (88.30)	20 (11.70)	.029	10 (5.85)	17 (9.94)
	Detroit	303	273 (90.10)	30 (9.90)		16 (5.28)	20 (6.60)
	Iowa	195	156 (80.00)	39 (20.00)		20 (10.26)	30 (15.38)
	Seattle	352	312 (88.64)	40 (11.36)		19 (5.40)	33 (9.38)
	Utah	284	255 (89.79)	29 (10.21)		8 (2.82)	24 (8.45)
	Connecticut	127	108 (85.04)	19 (14.96)		10 (7.87)	18 (14.17)
	San Jose	103	82 (79.61)	21 (20.39)		8 (7.77)	18 (17.48)
	Los Angeles	569	496 (87.17)	73 (12.83)		38 (6.68)	51 (8.96)
	Greater California	1171	987 (84.29)	183 (15.63)		89 (7.60)	149 (12.72)
	Kentucky	215	181 (84.19)	34 (15.81)		18 (8.37)	28 (13.02)
	Louisiana	316	276 (87.34)	40 (12.66)		23 (7.28)	29 (9.18)
	New Jersey	265	226 (85.28)	39 (14.72)		20 (7.55)	32 (12.08)
	New Mexico/Georgia /Hawaii	176	143 (81.25)	33 (18.75)		15 (8.52)	25 (14.20)
Population density	Metropolitan	3989	3430 (85.99)	558 (13.99)	.292	271 (6.79)	443 (11.11)
	Rural	258	216 (83.72)	42 (16.28)		23 (8.91)	31 (12.02)
Clinical stage	T1c	2218	1938 (87.38)	279 (12.58)	<.001	133 (6.00)	224 (10.10)
	T2	737	619 (83.99)	118 (16.01)		60 (8.14)	94 (12.75)
	T3	39	22 (56.41)	17 (43.59)		13 (33.33)	10 (25.64)
Gleason grade	≤6	1687	1599 (94.78)	88 (5.22)	<.001	29 (1.72)	71 (4.21)
	7	2073	1752 (84.52)	320 (15.44)		143 (6.90)	259 (12.49)
	≥8	469	280 (59.70)	189 (40.30)		120 (25.59)	143 (30.49)
PSA	<10	3141	2764 (88.00)	377 (12.00)	<.001	173 (5.51)	303 (9.65)
	10-20	495	391 (78.99)	104 (21.01)		49 (9.90)	84 (16.97)
	>20	170	117 (68.82)	53 (31.18)		33 (19.41)	39 (22.94)
Risk stratification	Low	1242	1188 (95.65)	54 (4.35)	<.001	17 (1.37)	41 (3.30)
	Intermediate	2265	1950 (86.09)	314 (13.86)		130 (5.74)	260 (11.48)
	High	637	408 (64.05)	229 (35.95)		146 (22.92)	171 (26.84)

SEER indicates Surveillance, Epidemiology, and End Results; PSA, prostate-specific antigen.
Data are presented as No. (%).

Table 2. Adjuvant Therapy by Surgeon Volume, Surgical Approach, Pathological Stage, and Surgical Margin

Independent Variable	Category	n	Adjuvant Therapy	Hormonal or Radiation	*P*	Hormonal Therapy	Radiation Therapy
Pathological stage	T2	3547	3201 (90.25)	345 (9.73)	<.001	148 (4.17)	275 (7.75)
	T3a	700	445 (63.57)	255 (36.43)		146 (20.86)	199 (28.43)
Positive surgical margin	Yes	822	563 (68.49)	259 (31.51)	<.001	129 (15.69)	213 (25.91)
	No	3425	3083 (90.01)	341 (9.96)		165 (4.82)	261 (7.62)
Surgeon volume in quartiles (no. of surgeons by approach)	Low (MIRP, 85; RRP, 396)	1027	867 (84.42)	159 (15.48)	.001	63 (6.13)	134 (13.05)
	Intermediate (MIRP, 21; RRP, 169)	1130	944 (83.54)	186 (16.46)		94 (8.32)	149 (13.19)
	High (MIRP, 12; RRP, 91)	1159	998 (86.11)	161 (13.89)		90 (7.77)	120 (10.35)
	Very high (MIRP, <11[a]; RRP, 37)	931	837 (89.90)	94 (10.10)		47 (5.05)	71 (7.63)
Surgical approach	MIRP	1120	998 (89.11)	122 (10.89)	<.001	59 (5.27)	97 (8.66)
	RRP	3127	2648 (84.68)	478 (15.29)		235 (7.52)	377 (12.06)
Positive lymph nodes	Yes	45	11 (24.44)	34 (75.56)	<.001	31 (68.89)	11 (24.44)
	No	4201	3635 (86.53)	566 (13.47)		263 (6.26)	463 (11.02)

MIRP indicates minimally invasive radical prostatectomy; RRP, retropubic radical prostatectomy.
Data are presented as No. (%).
[a] The actual number of MIRP surgeons is not presented because the National Cancer Institute precludes the reporting of table cells of n<11.

diagnosis. We then subtracted baseline health care expenditures, allowing subjects to serve as their own controls. We considered the difference in health expenditures between men receiving adjuvant treatment versus RP alone to be the health care expenditures attributable to hormonal therapy, radiotherapy, and both treatments in combination. Moreover, the health care expenditures included therapies, consultations, imaging, laboratory tests, and treatment of complications. All costs were adjusted to 2008 dollars using the 2007 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Fund.[22]

Statistical Analysis

Unadjusted analysis using the Pearson chi-square statistic was performed to compare demographic and biopsy tumor characteristics for patients receiving RP and adjuvant treatment versus RP alone, adjusting for clustering by surgeon, surgical approach, surgeon volume, and clinical characteristics.[23] A 2-sided result of $P<.05$ was considered statistically significant. Adjusted analysis was performed with a Cox multivariable regression model to assess the association of the covariates on the use of adjuvant therapies.

All tests were considered statistically significant at $\alpha = 0.05$. All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC).

RESULTS

The demographics of our study population are summarized in Table 1. We observed a temporal trend in the administration of adjuvant therapy after RP; patients were more likely to receive adjuvant therapy after RP performed in 2004 versus 2005 or 2006 (15.5%, 13.7% and 10.5%, $P = .028$). Moreover, whereas age, comorbidities, income, and education were not associated with receipt of adjuvant therapies, there was significant geographic variation for utilization of adjuvant therapies, with the San Jose versus Detroit region having the highest versus lowest utilization rates (20.4% vs 9.9%, $P<.001$). Furthermore, more aggressive tumor characteristics (higher Gleason grade, preoperative PSA, clinical stage, and risk stratification) were associated with receipt of adjuvant cancer therapy (all $P<.001$).

In assessing the effect of surgical approach, surgeon volume, and pathological features on the use of adjuvant therapies (Table 2), patients undergoing minimally invasive RP versus retropubic RP were less likely to receive additional cancer therapy (10.9% vs 15.3%, $P<.001$), and higher surgeon volume was associated with lower utilization of adjuvant cancer therapy ($P = .001$). Moreover, patients with pathological stage T3a versus T2 disease were more likely to receive additional therapy (36.4% vs 9.7%, $P<.001$), and patients with positive versus negative surgical margins were more likely to receive adjuvant cancer therapy (31.5% vs 10.0%, $P<.001$). Finally, patients with positive lymph nodes were more likely to receive adjuvant therapy (75.6% vs 13.5%, $P<.001$).

Table 3. Unadjusted and Adjusted Model for Predictors of Adjuvant Cancer Treatment

Covariate (Referent)	Categories	Univariate HR (95% CI)	Multivariate HR (95% CI)	Multivariate *P*
Age (≥75 years)	65-69	0.98 (0.71-1.34)	1.12 (0.81-1.55)	.477
	70-74	0.9 (0.65-1.26)	0.96 (0.69-1.35)	.823
Race (white)	Black	1.01 (0.74-1.39)	1.11 (0.79-1.55)	.555
	Hispanic	0.91 (0.67-1.24)	0.85 (0.62-1.17)	.316
	Asian	1.47 (1.05-2.06)	1.26 (0.88-1.8)	.203
SEER region (San Francisco)	20 = Michigan	0.89 (0.5-1.56)	0.90 (0.51-1.6)	.723
	22 = Iowa	1.76 (1.01-3.06)	1.93 (1.12-3.32)	.019
	25 = Seattle	1.82 (1.06-3.11)	1.10 (0.64-1.89)	.738
	26 = Utah	1 (0.58-1.7)	1.16 (0.65-2.08)	.612
	2 = Connecticut	0.94 (0.53-1.65)	1.37 (0.73-2.58)	.323
	31 = San Jose	1.32 (0.71-2.48)	1.71 (0.92-3.17)	.089
	35 = Los Angeles	1.82 (0.98-3.35)	1.30 (0.79-2.14)	.307
	41 = Greater California	1.15 (0.7-1.89)	1.48 (0.93-2.36)	.098
	42 = Kentucky	1.39 (0.87-2.2)	1.40 (0.8-2.45)	.233
	43 = Louisiana	1.41 (0.81-2.44)	1.33 (0.77-2.3)	.301
	44 = New Jersey	1.14 (0.67-1.95)	1.51 (0.87-2.61)	.141
	New Mexico/Georgia/Hawaii	1.33 (0.77-2.28)	1.92 (1.09-3.39)	.025
Risk stratification (low)	Intermediate	3.34 (2.5-4.46)	2.86 (2.14-3.83)	.001
	High	10.28 (7.64-13.84)	7.65 (5.64-10.37)	<.001
Surgical margin (negative)	Positive	3.65 (3.1-4.29)	3.02 (2.55-3.57)	<.001
Lymph nodes (negative)	Positive	12.73 (8.99-18.02)	5.36 (3.71-7.75)	<.001
Surgical approach (RRP)	MIRP	0.72 (0.59-0.88)	0.89 (0.72-1.1)	.285
Surgeon volume (low)	Intermediate	1.06 (0.86-1.31)	1.02 (0.82-1.27)	.855
	High	0.89 (0.72-1.11)	0.86 (0.69-1.08)	.203
	Very high	0.64 (0.49-0.82)	0.60 (0.46-0.78)	<.001
Year (2004)	2005	1 (0.85-1.19)	0.99 (0.83-1.18)	.903
	2006	0.85 (0.61-1.18)	0.86 (0.62-1.19)	.356

HR indicates hazard ratio; CI, confidence interval; RRP, retropubic radical prostatectomy; MIRP, minimally invasive radical prostatectomy.

In adjusted analysis (Table 3), age, race, marital status, and surgical approach (minimally invasive RP vs retropubic RP) were not significantly associated with receipt of adjuvant therapies. However, risk stratification was significantly associated with use of adjuvant therapies as patients with intermediate (hazard ratio [HR], 2.86; 95% confidence interval [CI], 2.14-3.83 [$P<.001$]) and high-risk (HR, 8.3; 6.13-11.22 [$P<.001$]) versus low-risk disease were more than 2 and 8 times more likely to undergo adjuvant therapies. Survival estimates are shown in Figure 1 for the various risk groups. Men undergoing RP by very high-volume surgeons were less likely to receive adjuvant therapies (HR, 0.64; 95% CI, 0.49-0.84 [$P = .001$]). Moreover, patients with positive versus negative surgical margins were 3 times more likely to undergo adjuvant therapies (HR, 3.2; 95% CI, 2.71-3.78 [$P<.001$]). Men with positive versus negative lymph nodes were 5 times more likely to receive adjuvant therapies (HR, 5.36; 95% CI, 3.71-7.75 [$P<.001$]). In addition, there was greater use of adjuvant therapies in Iowa (HR, 1.93; 95% CI, 1.12-3.32 [$P = .019$]) and New Mexico/Georgia/Hawaii (HR, 1.92; 95% CI, 1.09-3.39 [$P = .025$]) versus San Francisco SEER regions.

Baseline health care expenditures in the 12 months prior to prostate cancer diagnosis did not differ for patients who underwent RP alone versus adjuvant therapies of hormonal therapy, radiation therapy, and hormone and radiation therapy. However, the 12-month post–prostate cancer diagnosis health care expenditures (Table 4) of patients who underwent RP alone versus adjuvant therapies of hormonal therapy, radiation therapy, and combination hormonal and radiation therapy were significantly greater for adjuvant therapies ($P<.001$).

DISCUSSION

Approximately 13%-34% of men who undergo prostatectomy will have adverse pathological features such as positive surgical margins or extracapsular extension/pT3a disease.[24,25] There is a lack of consensus regarding when to initiate treatment in such patients; however, 22%-34% of these patients will receive salvage secondary treatments within 3 years of BCR.[26,27] Whereas a recent population-based study demonstrated significantly greater use of additional cancer treatments (eg, radiation and/or hormonal therapy), within 6 months of minimally invasive

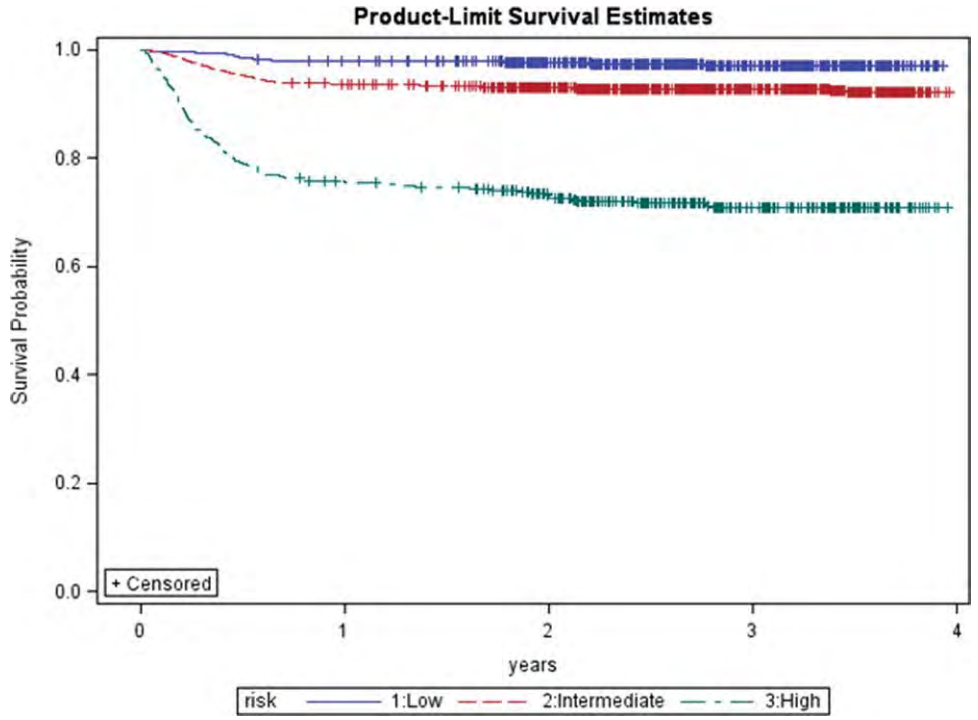

Figure 1. Estimated time to adjuvant therapy for the 3 risk groups with the number of subjects at risk at 1, 2, 3, and 4 years.

versus open RP, potential confounders such as surgical margin status and pathological stage and grade were unavailable in this analysis of Medicare beneficiaries.[16] In addition, there is an absence of population-based studies that assess use of adjuvant treatments after adjusting for surgical approach and surgeon volume. Aside from the lack of definitive guidelines on when to initiate adjuvant treatments after BCR and the appropriateness thereof, there is also concern of the added health care costs when adjuvant therapies are initiated.

Our paper has several important findings. First, higher surgeon volume was associated with decreased utilization of adjuvant cancer therapy independent of tumor characteristics. These findings would suggest that heterogeneity in practice patterns exist and that there is not uniform standardization of care. More experienced surgeons may prefer to manage positive surgical margins and extracapsular extension conservatively with surveillance versus adjuvant therapy. Similarly, Bianco et al.[28] found significant heterogeneity among BCR rates after adjusting for tumor characteristics and surgeon experience, and oncological outcomes vary due to measured and unmeasured characteristics of the treating surgeon. Thus, as Bianco et al. alluded to, there must be unmeasured characteristics of high-volume surgeons that result in decreased use of adjuvant therapies.

Second, we found that risk stratification was a significant predictor of adjuvant therapy use. Intermediate to high risk patients were approximately 3 to 8 times more likely to receive adjuvant therapy. Tumor biology as measured by pathological stage and grade have been previously shown to be powerful predictors for additional cancer therapy, whereas other patient variables including age and comorbidity have not.[12] Moreover, rapid PSA doubling time has also been shown to be significant predictors for secondary therapies.[29] Unfortunately, these endpoints are not captured in SEER-Medicare.

Third, positive surgical margin status was associated with increased utilization of adjuvant therapies, despite mixed evidence available during our study period regarding the impact of positive surgical margins on cancer recurrence and survival.[30] However, recently published randomized control trials demonstrate survival benefit from early adjuvant radiotherapy for positive surgical margins and high-risk features.[5,31] The interpretation of these trials is not without ongoing controversy, and further studies are warranted to clarify which patients would benefit most from adjuvant treatment.[32] Furthermore,

Table 4. Cost Analysis of Adjuvant Cancer Treatments

	Radical Prostatectomy	Radical Prostatectomy and Hormonal Therapy	Radical Prostatectomy and Radiation	Radical Prostatectomy and Radiation with Hormonal Therapy	*P*
Baseline health care expenditures in the year prior to prostate cancer diagnosis, median	$1861	$1272	$1380	$1333	.011
1-year postprostatectomy health care expenditures,[a] median	$15,022	$17,661			
	$28,442	$39,842	<.001		
Health care expenditures attributed to adjuvant therapies[b]	—	$1367	$12,040	$23,487	<.001

[a] We excluded patients who underwent radical prostatectomy and adjuvant therapies >6 months after initial treatment (radical prostatectomy) to ensure that we fully captured the expense associated with primary and adjuvant therapy.
[b] 1-year pre–prostate cancer diagnosis expenditures and expenditures of radical prostatectomy alone, respectively subtracted from 12-month postprostatectomy health care expenditures of various adjuvant therapies.

patients with lymph node–positive disease were more likely to receive adjuvant therapy, an increase that may be explained by prior studies demonstrating improved cancer-specific survival in such patients managed with adjuvant therapy.[33,34] With greater dissemination of evidence in favor of early adjuvant radiotherapy for adverse pathological features, more widespread adjuvant therapy use is expected and our results may underestimate current and future utilization of adjuvant therapies as practice patterns evolve.

Fourth, patient age, comorbidity status, and race were not significant predictors of adjuvant cancer therapy, consistent with previous studies.[11,12,29] One would expect that patient factors such as older age and more comorbidities would decrease the likelihood of receiving adjuvant therapies if treatment decisions were individualized. Moreover, these findings may highlight the need for guidelines based on life expectancy and postprostatectomy nomograms to better stratify which patients benefit most from adjuvant therapy. In addition, surgical approach was not a significant predictor for adjuvant therapy on multivariate analysis. Our findings contradict other studies that demonstrated greater use of secondary therapies following minimally invasive versus open RP, whereas other studies found no difference.[16,35] This difference may result from differences between the study populations: namely, a 5% random sample of Medicare beneficiaries[16] versus 100% of the Medicare beneficiaries in SEER tumor registry regions. Our study captures the entire surgeon Medicare experience in SEER regions versus a national 5% sampling of surgeon Medicare experience.

Finally, health care expenditures were $23,487 higher for combination radiation and hormonal therapy versus no treatment following prostatectomy. The additional expenditures for adjuvant hormonal therapy and radiotherapy were $1367 and $12,040, respectively versus RP alone. In particular, positive surgical margins, a surgeon-dependent variable, may increase the cost of cancer therapy significantly, particularly after level 1 evidence of improved survival from secondary radiation therapy.[4–6]

Our findings must be interpreted within the context of the study design. First, Medicare is limited to patients ≥65 years of age, and nerve-sparing may be performed more frequently in younger, potent men.[36] This factor, combined with the absence of margin status for pathological stage T3b and T4 disease, may lead to underestimation of the overall prevalence of adjuvant cancer treatments in patients undergoing RP.[24] Second, the SEER tumor registry does not contain detailed clinical information on PSA or biochemical recurrence, tumor volume, perineural invasion, and tertiary high Gleason grade, factors that increase the likelihood of adjuvant therapy use.[37–39] Third, we were unable to determine whether adjuvant radiotherapy was administered in an adjuvant versus salvage fashion, because postprostatectomy PSA data were unavailable. This observation is noteworthy, because initiation of adjuvant therapies is influenced by variation in provider practice patterns, whereas initiation of salvage therapy may be influenced by variations in PSA biochemical recurrence thresholds. Finally, our estimates of adjuvant therapy expenditures are lower than expenditures by private health plans versus Medicare.

Conclusions

Higher surgeon volume and geographic variation was independently associated with decreased use of additional therapy, demonstrating physician and regional practice pattern heterogeneity. Patients undergoing RP were

significantly more likely to undergo adjuvant treatments in the presence of higher risk stratification and positive surgical margins. Finally, adjuvant therapies significantly increased cancer-specific health care expenditures by 2- to 3-fold when radiotherapy was administered postoperatively.

Supplementary material for this article can be obtained at http://physiciandirectory.brighamandwomens.org/directory/profile.asp?dbasemain&setsize30&last_namehu&pict_id0009649.

CONFLICT OF INTEREST DISCLOSURES

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BJUI BJU INTERNATIONAL

Population-based determinants of radical prostatectomy surgical margin positivity

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Study Type – Prognosis (cohort)
Level of Evidence 2b

What's known on the subject? and What does the study add?
Prior population and single-centre studies have assessed incidence of positive surgical margins. The current study derived population-based positive surgical margin cut-offs in order to help identify underperforming surgeons who may benefit from further courses and/or self study to improve outcomes.

OBJECTIVE

- To characterize factors associated with positive surgical margins (PSMs) and derive population-based PSM cutoffs to evaluate surgeon performance in radical prostatectomy (RP).

PATIENTS AND METHODS

- SEER-Medicare data were used to identify 4247 men diagnosed with prostate cancer during 2004–2005 who underwent RP up to 2006.
- We performed logistic regression to assess the impact of tumour characteristics, surgeon volume and surgical approach on the likelihood of PSMs for pT2 and PT3a disease.
- Moreover, we derived 25th and 10th percentile cutoffs from binomial distribution equations.

RESULTS

- Overall, 19.4% of men experienced PSMs with a pT2 vs pT3a PSM rate of 14.9% vs 42% ($P < 0.001$). Extrapolating from our population-based results, a surgeon incurring more than three PSMs in 10 cases of pT2 disease performed below the 25th percentile.
- There was a trend for fewer PSMs with minimally invasive vs open RP (17.4% vs 20.1%, $P = 0.086$), and the PSM rate also decreased over the study period from 21.3% in 2004 to 16.6% in 2006 ($P = 0.028$) with significant geographic variation ($P < 0.001$).
- In adjusted analyses, temporal and geographic variation in PSM persisted, and men with high (odds ratio 3.68, 95% CI 2.82–4.81) and intermediate (odds ratio 2.52, 95% CI 2.03–3.13) vs low-risk disease were at greater odds to experience PSMs. Notably, neither surgical approach nor surgeon volume was significantly associated with PSMs.

CONCLUSION

- Our population-based PSM benchmarks allow identification of under-performing outliers who may seek courses or video self-study to improve outcomes. There was significant temporal and geographic variation in PSMs but neither surgeon volume nor surgical approach was associated with PSMs.

KEYWORDS

positive margins, prostatectomy, minimally invasive, surgeon volume, outcomes

INTRODUCTION

Positive surgical margin status is a significant predictor of biochemical recurrence after radical prostatectomy [1]. Although positive surgical margins and greater PSA velocity, tumour grade and stage are associated with an increased risk of prostate cancer recurrence, only surgical margin status is influenced by surgical technique. In addition, positive surgical margins for organ-confined prostate cancer may serve as a quality indicator, and recent level 1 evidence shows a survival advantage when adjuvant radiotherapy is administered to counter this undesirable outcome [2,3]. Consequently, positive surgical margins increase the cost of treating prostate cancer secondary to the use of adjuvant radiotherapy and treatment of cancer recurrence.

Minimally invasive radical prostatectomy with and without robotic assistance has been rapidly adopted [4] but there are few comparisons of surgical margin status in minimally invasive surgery with that in open retropubic radical prostatectomy aside from single-centre studies [5]. Furthermore, some contend that the sense of palpation during retropubic radical prostatectomy, which is lacking with the minimally invasive approach, allows better assessment of the extent of tumour [6], potentially resulting in fewer positive margins and better cancer control. Our study objectives were: to characterize determinants of positive surgical margins and to derive population-based positive surgical margin benchmarks for surgeon self-assessment.

PATIENTS AND METHODS

Surveillance, Epidemiology, and End Results (SEER)–Medicare data were used for analyses, which comprise a linkage of population-based cancer registry data from 16 SEER areas covering approximately 26% of the US population with Medicare administrative

TABLE 1 Demographics of the study population

Characteristic	Categories	Total	Positive margin, *n* (%)	*P*-value
Year of surgery	2004	1779	378 (21.3)	0.028
	2005	2058	376 (18.3)	
	2006	410	68 (16.6)	
Age (years)	65–69	2620	485 (18.5)	0.203
	70–74	1332	270 (20.3)	
	≥75	295	67 (22.7)	
Charlson comorbidity index	0	2956	554 (18.7)	0.080
	1	1018	202 (19.8)	
	≥2	273	66 (24.2)	
Race	White	3366	661 (19.6)	0.932
	Black	307	57 (18.6)	
	Hispanic	356	64 (18.0)	
	Asian	186	34 (18.3)	
	Other	32	6 (18.8)	
Marital status	Unmarried	605	102 (16.9)	0.031
	Married	3469	694 (20.0)	
	Unknown	173	26 (15.0)	
Education: % of census tract with at least a high school degree	<75	785	142 (18.1)	0.108
	75–84.99	785	131 (16.7)	
	85–89.99	791	159 (20.1)	
	≥90	1885	389 (20.6)	
Median income in census tract of residence	<$35 000	1106	203 (18.35)	0.321
	$35 000–44 000	975	188 (19.28)	
	$45 000–59 000	1072	227 (21.18)	
	≥$60 000	1093	203 (18.57)	
SEER region	San Francisco	171	31 (18.13)	<0.001
	Detroit	303	59 (19.47)	
	Iowa	195	46 (23.6)	
	Seattle	352	85 (24.15)	
	Utah	284	78 (27.5)	
	Connecticut	127	27 (21.26)	
	San Jose	103	21 (20.39)	
	Los Angele	569	137 (24.08)	
	Greater Ca	1171	232 (19.81)	
	Kentucky	215	31 (14.42)	
	Louisiana	316	43 (13.61)	
	New Jersey	265	13 (4.9)	
	New Mexico/Georgia/Hawaii	176	19 (10.80)	
Population density	Metropolitan	3989	773 (19.38)	0.891
	Rural	258	49 (18.99)	
Clinical stage	T1c	2218	408 (18.39)	0.452
	T2	737	148 (20.08)	
	T3	39	9 (23.08)	
	Unknown	1253	257 (20.51)	
Gleason grade	≤ 6	1687	190 (11.26)	<0.001
	7	2073	487 (23.49)	
	≥8	469	144 (30.70)	
	Unknown	18	1 (5.56)	
PSA	<10	3141	568 (18.08)	0.0001
	10–20	495	123 (24.85)	
	>20	170	47 (27.65)	
	Unknown	441	84 (19.05)	
D'Amico risk	Low	1242	130 (10.47)	<0.001
	Intermediate	2265	502 (22.16)	
	High	637	177 (27.79)	
	Unknown	103	13 (12.62)	

PSA, prostate-specific antigen; SEER, surveillance, epidemiology, and end results.

data. The Medicare programme provides benefits to most Americans aged ≥65 years.

We identified 6153 men aged ≥65 years enrolled in Medicare Parts A and B, not enrolled in the Medicare health maintenance organization (because their claims were not reliably submitted), diagnosed with prostate cancer in 2004 and 2005 who underwent open and minimally invasive radical prostatectomy from 2004 to 2006. We stratified the surgical approach on the basis of the Physicians Current Procedural Terminology Coding System 4th edition, (CPT-4): 55840, 55842, 55845 for open retropubic radical prostatectomy; and 55866 for minimally invasive radical prostatectomy [4,7]. Because SEER only captures positive margin characteristics for the American Joint Commission on Cancer pathological T2 and T3a disease, we excluded 293 men with pathological stage T3b, 63 men with pathological T4 and 1132 men with missing pathological information. We also excluded 318 men who underwent radical prostatectomy outside SEER regions to avoid misclassification of surgeon volume.

The control variables were obtained as follows. Patient age was obtained from the Medicare file; race, census tract measures of median household income and high school education, Census region, population density (urban vs rural), and marital status were obtained from SEER registry data. Comorbidity was assessed using the Klabunde modification of the Charlson index during the year before surgery [8]. Variables were categorized as in Table 1. Additionally, we used PSA, Gleason Grade and stage to stratify men to low-risk, intermediate-risk and high-risk disease [9]. However, clinical tumour stage was missing/unknown for almost one-third of our subjects. Moreover, there was a lower than expected percentage of men (18%) in the low-risk group compared with a community cohort [10]. We hypothesized that biopsy findings, rather than indication for biopsy, may have to be used for clinical staging, contrary to American Joint Committee on Cancer guidelines. We therefore used a modified D'Amico risk stratification that omitted clinical stage, resulting in a low-risk designation for 29% of our cohort.

Because surgeon rather than hospital volume is the more significant determinant of outcomes after retropubic radical prostatectomy [11], we determined surgeon

TABLE 2 Surgical margin status by surgeon volume, surgical approach and pathological stage

Independent variable	Category	Total	Positive margin *n* (%)	*P*-value
Surgical approach	MIRP	1121	195 (17.4)	0.086
	RRP	3119	627 (20.1)	
Surgeon volume in quartiles (no. of surgeons by approach)	Low (MIRP 85; RRP 396)	1027	179 (17.43)	0.329
	Intermediate (MIRP 21; RRP 169)	1130	217 (19.20)	
	High (MIRP 12; RRP 91)	1159	228 (19.67)	
	Very high (MIRP < 11*; RRP 37)	931	198 (21.27)	
Pathological stage	T2	3544	528 (14.9)	<0.001
	T3a	700	294 (42.0)	

MIRP, minimally invasive radical prostatectomy; RRP, radical retropubic prostatectomy.
**Actual number of MIRP surgeons not presented because the National Cancer Institute precludes the reporting of table cells of* n < *11.*

volume by aggregating the number of procedures performed from 2004 to 2006. We assessed surgeon volume a priori as both a continuous and a categorical variable. Categorically, surgeon volume for the study period was divided into quartiles, consistent with a previous study [12], corresponding to 1–7 radical prostatectomies for low, 8–15 for intermediate, 16–29 for high, and 30–91 for very high for open radical prostatectomy surgeons. On the other hand, the minimally invasive radical prostatectomy surgeon volume quartile distribution over the study period was 1–14 radical prostatectomies for low, 15–36 for intermediate, 37–89 for high, and 90–218 for very high volume surgeons.

In sub-analyses, we analysed the effect of surgeon volume on minimally invasive and open radical prostatectomy surgical margin positivity, respectively, and did not find a significant relationship. Finally, we stratified surgical approach into minimally invasive vs open radical prostatectomy.

Bivariate analyses were performed to compare patient characteristics and positive surgical margin status by surgeon volume using the Rao-Scott–Pearson chi-squared statistic, which accounts for clustering by surgeon [13]. A Rao-Scott–Pearson chi-squared test was also used to compare the overall positive margin by surgical approach. Logistic regression was performed to determine the effect of surgeon volume as a continuous and categorical variable; logistic regression was also used to assess the effect of age, race, SEER region, surgical approach, D'Amico risk stratification, and year of surgery on positive surgical margins. For the logistic regressions, generalized estimating equations were used to account for clustering of patients by surgeon [14]. All tests were considered statistically significant at $\alpha = 0.05$. All analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, NC, USA).

To derive the 25th and 10th percentile positive surgical margin thresholds for a given urologist, using results from generalized linear mixed models (given a random urologist effect) [15], the number of operations with positive margins out of the N operations performed by a surgeon follows a binomial distribution. Because most practicing urologists perform fewer than 12 major operations a year including radical prostatectomy [16], we present postivie surgical margin performance thresholds for surgeon volumes of 5 to 12 radical prostatectomies. Moreover, given that 42% [17] of US radical prostatectomies are performed in men aged 65 years and older, we determined that 57.6% and 67.7% of minimally invasive radical prostatectomy surgeons performed fewer than 12 radical prostatectomies in 2004 and 2005 whereas 67.6% and 70.5% of open radical prostatectomy surgeons performed fewer than 12 radical prostatectomies in 2004 and 2005, respectively. Assuming that the probability of a positive margin equals the mean positive margin rate from our study population, the 25th and 10th percentiles for surgeon-specific positive margin rates out of N operations performed can be derived using the binomial distribution formula [18], with π as the mean population-based positive margin rate, and N as the number of operations performed. The exact percentiles can be obtained from the SAS 'quantile' function. A normal-based approximation to the percentiles can be obtained with the formulae [19]:

$$25\text{th percentile} = \pi + 1.5/N + 0.675\sqrt{\pi(1-\pi)/N}$$

$$10\text{th percentile} = \pi + 1.5/N + 1.28\sqrt{\pi(1-\pi)/N}$$

RESULTS

The demographics of our study population are presented in Table 1. The positive surgical margin rate decreased during the 3-year study period from 21.3% to 16.6% from 2004 to 2006. Although there were no significant associations between age, comorbidity and race and positive surgical margins, married men were more likely than unmarried men to experience positive surgical margins (20.0% vs 16.9%, $P = 0.031$). Moreover, there was significant geographic variation in positive surgical margin rates, ranging from 4.9% to 27.5% ($P < 0.001$). Finally, higher PSA level ($P < 0.001$) and Gleason grade ($P < 0.001$), and consequently higher risk disease ($P < 0.001$), were associated with higher positive surgical margin rates.

The relationships between surgical approach, surgeon volume and pathological stage with positive surgical margins are presented in Table 2. There was a trend for fewer positive surgical margins with minimally invasive vs retropubic radical prostatectomy (20.1% vs 17.4%, $P = 0.086$) but there was no association between overall surgeon volume with positive surgical margins. In addition, sub-analyses of minimally invasive and retropubic radical prostatectomy surgeon volume, respectively, did not reveal an association with positive surgical margins. However, the positive surgical margin rate

TABLE 3 Adjusted model for predictors of surgical margin positivity

Covariate (referent)	Categories	OR (95% CI)	*P*-value
Age (≥75 years)	65–69	1.01 (0.69–1.46)	0.978
	70–74	1.03 (0.71–1.48)	0.877
Race (White)	Black	1.19 (0.84–1.69)	0.333
	Hispanic	0.91 (0.68–1.23)	0.547
	Asian	0.88 (0.58–1.34)	0.556
D'Amico risk (Low)	Intermediate	2.52 (2.03–3.13)	<0.001
	High	3.68 (2.82–4.81)	<0.001
Surgical approach (RRP)	MIRP	0.93 (0.77–1.13)	0.464
Surgeon volume (Low)	Intermediate	1.0 (0.77–1.3)	0.989
	High	0.94 (0.74–1.18)	0.583
	Very high	1.02 (0.8–1.31)	0.845
SEER Region (San Francisco)	Detroit	1.16 (0.72–1.86)	0.534
	Iowa	1.41 (0.82–2.4)	0.213
	Seattle	1.43 (0.9–2.28)	0.125
	Utah	1.94 (1.17–3.22)	0.011
	Connecticut	1.23 (0.72–2.11)	0.451
	San Jose	1.24 (0.7–2.19)	0.460
	Los Angeles	1.56 (1.01–2.42)	0.047
	Greater California	1.17 (0.78–1.77)	0.440
	Kentucky	0.73 (0.42–1.26)	0.254
	Louisiana	0.68 (0.39–1.17)	0.160
	New Jersey	0.23 (0.12–0.43)	<0.001
	New Mexico/Georgia/Hawaii	0.54 (0.28–1.05)	0.071
Year (2004)	2005	0.83 (0.7–0.98)	0.033
	2006	0.75 (0.55–1.01)	0.057

95% CI, 95% confidence interval; MIRP, minimally invasive radical prostatectomy; OR, odds ratio; RRP, radical retropubic prostatectomy.

TABLE 4 Positive surgical margin percentile thresholds for surgeon volume of 5 to 12 radical prostatectomies based on binomial distribution and population means for pT2 and pT3a disease

Surgeon volume	Organ-confined disease, $\pi = 0.0149$ *n* cases with positive margins (%)		Extracapsular extension, $\pi = 0.420$ *n* cases with positive margins (%)	
N	25th percentile	10th percentile	25th percentile	10th percentile
5	2 (40)	3 (60)	4 (80)	5 (100)
6	2 (33)	3 (50)	4 (67)	5 (83)
7	3 (43)	3 (43)	5 (71)	6 (86)
8	3 (38)	4 (50)	5 (63)	6 (75)
9	3 (33)	4 (44)	6 (67)	7 (78)
10	3 (30)	4 (40)	6 (60)	7 (70)
11	3 (27)	4 (36)	7 (64)	8 (73)
12	4 (33)	5 (41)	7 (58)	8 (67)

Because of the discreteness of the binomial distribution, the cutoff rates are not identical for different surgeon volumes. Using the n values in this table, the 25th and 10th percentiles are actually (n – 1)/N, but to reduce confusion, because correction action may be undertaken if surgeon-specific positive margin rates exceed the 25th percentiles, this table includes the minimum thresholds for the above percentiles.

was higher for pT3a vs pT2 disease (42.0% vs 14.9%, $P < 0.001$).

The adjusted analyses are presented in Table 3. Men undergoing radical prostatectomy in 2005 vs 2004 experienced lower odds for positive surgical margins (odds ratio 0.83, 95% CI 0.7–0.98), and there was a trend for lower odds of positive surgical margins in 2006 vs 2004 (OR 0.75, 95% CI 0.55–1.01). Significant geographic variation in positive surgical margin rates persisted in adjusted analysis. Whereas men undergoing radical prostatectomy in New Jersey experienced lower odds of positive surgical margins (OR 0.23, 95% CI 0.12–0.43), those in Utah (OR 1.94, 95% CI 1.17–3.22) and Los Angeles (OR 1.56, 95% CI 1.01–2.42) experienced greater odds of positive surgical margins vs San Francisco (referent). Moreover, men with high-risk (OR 3.68 95% CI 2.82–4.81) and intermediate-risk (OR 2.52, 95% CI 2.03–3.13) vs low-risk features experienced greater odds of positive surgical margins. Notably, there was no association between surgeon volume stratified in quartiles and assessed as a continuous variable (Appendix) and likelihood of positive surgical margins.

Table 4 displays the 25th and 10th percentile positive margin rate thresholds for organ-confined disease based on the population-based pT2 positive margin rate of 14.9%. This is derived from the exact binomial for $\pi = 0.149$ and varying surgeon volumes (*N*). For example, a surgeon experiencing positive margins in 3 of 10 men with organ-confined disease would perform at the 25th percentile.

DISCUSSION

Population-based studies have shown that higher radical prostatectomy surgeon volume is associated with fewer in-hospital and late urinary complications, shorter lengths of stay, and less use of additional cancer therapy [4,11,12]. In addition, multicentre studies have characterized a learning curve for cancer control, as greater surgeon experience in open and minimally invasive radical prostatectomies portends fewer biochemical recurrences [20,21]. A recent population-based study showed significantly greater use of additional cancer treatments, i.e. radiation and/or hormonal therapy, within 6 months of minimally invasive vs open radical prostatectomy but potential confounders

such as surgical margin status and pathological stage and grade were unavailable [4]. Additionally, there is an absence of population-based studies that explore the potential influence of surgical approach and surgeon volume on positive margin status. Positive surgical margins increase patient distress and fear of cancer recurrence [22], and add to healthcare costs when adjuvant radiotherapy is added to improve cancer control [2,3].

Our paper has several important findings. First, we present population-based radical prostatectomy positive surgical margin rates of 14.9% for organ-confined disease and 42% for extracapsular extension. In addition, we derived positive surgical margin performance thresholds that may serve as benchmarks for surgeon self-assessment, rather than comparison with published positive margin rates from high-volume single surgeon series. Surgeons experiencing positive margin rates in excess of population-based benchmarks might review intraoperative video of themselves [23] or others and seek courses to improve their surgical technique and lower their positive margin rates. Although we present 25th and 10th percentile population-based positive margin thresholds, others may use the binomial distribution to individualize 'acceptable' performance levels.

Second, we observed lower positive surgical margin rates when comparing radical prostatectomies performed in 2005 vs 2004. There was a trend for lower positive surgical margin rates for 2006 than 2004 but the study might have been underpowered to detect significance because our study cohort comprised men diagnosed with prostate cancer through 2005 who had surgery in 2006, rather than including all men undergoing radical prostatectomy in 2006. Although a temporal trend for fewer positive surgical margins is consistent with the gradual diffusion of surgical technique and improved outcomes that follow [24,25], subsequent years of data, when available, must be analysed to determine if margin rates continue to decrease.

Third, we observed significant geographic variation in positive surgical margin rates. This parallels variations in positive surgical margin rates from single centre reports. Moreover, our regional differences in positive surgical margins parallel other population-based studies showing geographic variation in radical prostatectomy outcomes [11,24,26]. These findings underscore the heterogeneity in radical prostatectomy technique and outcomes. Moreover, we observed that married vs unmarried men experienced high surgical margin positivity; however, the inability to determine use of nerve-sparing technique from SEER-Medicare data prevents us from exploring this further.

Fourth, while there are purported advantages of tumour palpation and intraoperative decision-making on improved cancer control during open compared with minimally invasive radical prostatectomy [6], most US men with prostate cancer increasingly present with raised PSA levels and low-volume disease rather than with disease that is palpable on digital rectal examinations [10,27], and our population-based analyses show similar positive surgical margin rates between minimally invasive and open radical prostatectomy. Moreover, early cancer control was also similar for minimally invasive and open radical prostatectomy from a study of SEER-Medicare linked data [7]. Our findings contrast with those contending that men undergoing minimally invasive vs open radical prostatectomy experience inferior cancer control [4,28].

Finally, we did not observe a relationship between surgeon volume and positive surgical margin status. This contrasts two multicentre studies showing that higher surgeon volume was associated with lower positive margin rates [29,30]. However, individual surgeon characteristics and heterogeneity also affect surgical margin status; surgeon volume was no longer a predictor of surgical margin status after excluding the highest volume surgeon from one study [30] but positive margin rates for open radical prostatectomy surgeons at high volume, academic referral centres varied widely from 11% to 48% in the other study [29]. In addition, a recent multicentre study showed significant heterogeneity in cancer recurrence after adjusting for surgeon experience and tumour characteristics [31].

Our findings must be interpreted in the context of the study design. First, SEER-Medicare does not contain detailed clinical information regarding whether nerve-sparing technique was used, which increases the likelihood of positive surgical margins [32]. Second, Medicare is limited to men aged 65 years and older, and nerve-sparing may be performed more frequently in younger, potent men [32]. This, along with the absence of margin status for pathological T3b and T4 disease, may lead to underestimation of the overall prevalence of positive margins in all men undergoing radical prostatectomy, regardless of age. However, the number of men omitted with pathological T3b and T4 disease was relatively small, and positive margins in organ-confined vs extraprostatic disease may serve as a better litmus test for the quality of surgical technique. Third, heterogeneous pathological processing and interpretation may lead to variation in positive surgical margin status [2,3]. Fourth, we were unable to differentiate between minimally invasive radical prostatectomy performed with and without robotic assistance because both share a common CPT code; however, a recent survey showed a 75% reduction in volume among surgeons performing minimally invasive radical prostatectomy without robotic assistance [33], and the robot-assisted approach likely accounted for most of the minimally invasive radical prostatectomies. Finally, many cases and several years may transpire before low-volume surgeons can accurately characterize their positive margin rates stratified by tumour characteristics, and this may be a potential limitation of our margin positivity thresholds for surgical margin positivity because real-time feedback is unavailable.

Our population-based, organ confined (pT2) positive surgical margin rate of 14.9% and 25th and 10th percentile cutoffs may serve as a benchmark for radical prostatectomy surgeon self-assessment. Although we observed temporal improvement and significant geographic variation in positive surgical margin rates, we did not find a surgeon volume–outcomes effect with positive surgical margins, probably because of heterogeneity in the surgical technique. Finally, positive surgical margin rates were similar for minimally invasive and open radical prostatectomy.

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CONFLICT OF INTEREST

None declared.

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Abbreviations: **OR**, odds ratio; **SEER**, surveillance, epidemiology, and end results.

APPENDIX ADJUSTED MODEL OF PREDICTORS OF SURGICAL MARGIN POSITIVITY WITH SURGEON VOLUME AS A CONTINUOUS VARIABLE

Covariate (referent)	Categories	OR (95% CI)	*P*-value
Age (≥75 years)	65–69	1.01 (0.69–1.47)	0.975
	70–74	1.03 (0.71–1.49)	0.874
Race (White)	Black	1.19 (0.84–1.69)	0.335
	Hispanic	0.92 (0.68–1.24)	0.569
	Asian	0.89 (0.59–1.34)	0.567
D'Amico risk (Low)	Intermediate	2.5 (2.03–3.13)	<0.001
	High	3.7 (2.81–4.80)	<0.001
Surgical approach (RRP)	MIRP	0.91 (0.72–1.14)	0.404
Surgeon volume (continuous)	Per 10 surgeries	1.01 (0.99–1.02)	0.512
SEER region	Detroit	1.14 (0.72–1.82)	0.570
	Iowa	1.4 (0.82–2.38)	0.217
	Seattle	1.43 (0.91–2.25)	0.119
	Utah	1.91 (1.15–3.17)	0.012
	Connecticut	1.24 (0.73–2.12)	0.421
	San Jose	1.23 (0.7–2.19)	0.469
	Los Angeles	1.55 (1–2.4)	0.051
	Greater California	1.17 (0.78–1.75)	0.445
	Kentucky	0.73 (0.42–1.25)	0.251
	Louisiana	0.68 (0.4–1.15)	0.152
	New Jersey	0.23 (0.12–0.43)	<0.001
	New Mexico/Georgia/Hawaii	0.55 (0.28–1.06)	0.074
Year (2004)	2005	0.83 (0.7–0.98)	0.033
	2006	0.75 (0.56–1.01)	0.059

95% CI, 95% confidence interval; MIRP, minimally invasive radical prostatectomy; OR, odds ratio; RRP, radical retropubic prostatectomy.

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ORIGINAL REPORT

Cost Implications of the Rapid Adoption of Newer Technologies for Treating Prostate Cancer

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See accompanying editorial on page 1503

A B S T R A C T

Purpose
Intensity-modulated radiation therapy (IMRT) and laparoscopic or robotic minimally invasive radical prostatectomy (MIRP) are costlier alternatives to three-dimensional conformal radiation therapy (3D-CRT) and open radical prostatectomy for treating prostate cancer. We assessed temporal trends in their utilization and their impact on national health care spending.

Methods
Using Surveillance, Epidemiology, and End Results–Medicare linked data, we determined treatment patterns for 45,636 men age ≥ 65 years who received definitive surgery or radiation for localized prostate cancer diagnosed from 2002 to 2005. Costs attributable to prostate cancer care were the difference in Medicare payments in the year after versus the year before diagnosis.

Results
Patients received surgery (26%), external RT (38%), or brachytherapy with or without RT (36%). Among surgical patients, MIRP utilization increased substantially (1.5% among 2002 diagnoses *v* 28.7% among 2005 diagnoses, $P < .001$). For RT, IMRT utilization increased substantially (28.7% *v* 81.7%; $P < .001$) and for men receiving brachytherapy, supplemental IMRT increased significantly (8.5% *v* 31.1%; $P < .001$). The mean incremental cost of IMRT versus 3D-CRT was $10,986 (in 2008 dollars); of brachytherapy plus IMRT versus brachytherapy plus 3D-CRT was $10,789; of MIRP versus open RP was $293. Extrapolating these figures to the total US population results in excess spending of $282 million for IMRT, $59 million for brachytherapy plus IMRT, and $4 million for MIRP, compared to less costly alternatives for men diagnosed in 2005.

Conclusion
Costlier prostate cancer therapies were rapidly and widely adopted, resulting in additional national spending of more than $350 million among men diagnosed in 2005 and suggesting the need for comparative effectiveness research to weigh their costs against their benefits.

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INTRODUCTION

With approximately 180,000 new diagnoses per year,[1] prostate cancer has been cited as a litmus test for health care spending and reform due to its rising costs of care.[2] Over the past decade, newer and more expensive alternatives have been introduced for the treatment of prostate cancer. For men who choose surgery, minimally invasive radical prostatectomy (MIRP), which includes either laparoscopic or robotic-assisted surgery, is a costlier alternative to the traditional open RP due to the greater cost of disposables, equipment, and increased operating room time during a lengthy learning curve.[3] For men who choose radiation, intensity-modulated radiation therapy (IMRT) is a more expensive alternative to traditional three-dimensional conformal radiation therapy (3D-CRT) due to more intense physics planning and quality assurance time, as well as treatment delivery time and software and hardware costs.[4]

Despite interest from patients and providers in these newer technologies, and belief by advocates that they could improve outcomes, there was only limited comparative effectiveness data when they were introduced, and to date there have been no randomized trials testing their clinical efficacy compared to traditional, less expensive counterparts. The purpose of this study is to characterize the adoption of these more expensive therapies among Medicare beneficiaries and to estimate the excess health

Table 1. Baseline Patient Characteristics Stratified by Primary Curative Modality Chosen

Variable	Brachytherapy		External RT		Surgery		*P*
	No.	%	No.	%	No.	%	
Race							
White	13,247	80.44	13,326	77.14	9,498	79.86	< .001
Black	1,470	8.93	1,716	9.93	910	7.65	
Hispanic	842	5.11	1,058	6.12	904	7.60	
Asian	592	3.59	795	4.60	441	3.71	
Other/unknown	317	1.92	379	2.19	141	1.19	
Age at diagnosis, years							
65-69	5,591	33.95	3,969	22.98	7,435	62.51	< .0001
70-74	5,915	35.92	5,793	33.54	3,589	30.17	
75-79	4,962	30.13	7,512	43.49	870	7.31	
High school education in patient's census region, %							
< 75/unknown	3,453	20.97	3,906	22.61	2,377	19.98	< .0001
75-84	3,546	21.53	4,064	23.53	2,368	19.91	
85-89	3,118	18.93	3,255	18.84	2,213	18.61	
90+	6,351	38.57	6,049	35.02	4,936	41.50	
Median income, $							
< 35,000/unknown	5,244	31.85	6,686	38.70	3,590	30.18	< .0001
35,000-44,000	3,905	23.71	4,017	23.25	2,812	23.64	
45,000-59,000	3,921	23.81	3,634	21.04	2,736	23.00	
≥ 60,000	3,398	20.63	2,937	17.00	2,756	23.17	
Region*							
Northeast	4,936	29.97	4,362	25.25	1,414	11.89	< .0001
South	3,365	20.43	2,733	15.82	1,975	16.61	
Midwest	1,751	10.63	3,202	18.54	1,634	13.74	
West	6,416	38.96	6,977	40.39	6,871	57.77	
SEER registry							
San Francisco	605	3.67	592	3.43	488	4.10	< .0001
Michigan	1,137	6.90	2,029	11.75	916	7.70	
New Mexico/Georgia/Hawaii	1,526	9.27	1,145	6.63	770	6.47	
Iowa	614	3.73	1,173	6.79	718	6.04	
Seattle	1,092	6.63	745	4.31	909	7.64	
Utah	959	5.82	209	1.21	693	5.83	
Connecticut	978	5.94	1,552	8.98	448	3.77	
San Jose	433	2.63	375	2.17	246	2.07	
Los Angele	672	4.08	1,283	7.43	1,275	10.72	
Greater California	2,199	13.35	2,943	17.04	2,742	23.05	
Kentucky	1,178	7.15	1,261	7.30	684	5.75	
Louisiana	1,117	6.78	1,157	6.70	1,039	8.74	
New Jersey	3,958	24.03	2,810	16.27	966	8.12	
Population density							
Metropolitan	15,192	92.25	15,619	90.42	10,896	91.61	< .0001
Nonmetropolitan	1,276	7.75	1,655	9.58	998	8.39	
Marital status							
Not married	3,024	18.36	3,579	20.72	1,792	15.07	< .0001
Married	12,106	73.51	11,959	69.23	9,509	79.95	
Unknown	1,338	8.12	1,736	10.05	593	4.99	
Grade							
Well	224	1.36	224	1.30	158	1.33	< .001
Moderate	11,067	67.20	9,210	53.32	6,451	54.24	
Poorly/undifferentiated	4,849	29.44	7,530	43.59	5,211	43.81	
Unknown	328	1.99	310	1.79	74	0.62	
Clinical stage							
T1	7,880	47.85	7,246	41.95	5,149	43.29	< .001
T2	8,049	48.88	8,905	51.55	6,365	53.51	
T3	267	1.62	603	3.49	174	1.46	
T4	16	0.10	137	0.79	21	0.18	
Unknown	256	1.55	383	2.22	185	1.56	

(continued on following page)

Table 1. Baseline Patient Characteristics Stratified by Primary Curative Modality Chosen (continued)

Variable	Brachytherapy		External RT		Surgery		
	No.	%	No.	%	No.	%	*P*
Charlson score							
0	11,860	72.02	11,516	66.67	9,412	79.13	< .001
1	3,230	19.61	3,765	21.80	1,760	14.80	
2+	1,153	7.00	1,763	10.21	448	3.77	
Unknown	225	1.37	230	1.33	274	2.30	
Total	16,468	36	17,274	38	11,894	26	

NOTE. Education had 24 unknown, income had 26 unknown. For men diagnosed in 2002, well differentiated refers to a Gleason score of 2-4, moderately differentiated is Gleason 5-7, and poorly differentiated is Gleason 8-10, but for men diagnosed from January 1, 2003 onward, poorly differentiated was designated as Gleason 7. Region categorization: northeast: Connecticut and New Jersey; south, Atlanta, rural Georgia, Kentucky, and Louisiana; west: San Francisco, Hawaii, New Mexico, Seattle, Utah, San Jose, Los Angeles, and greater California; and midwest: Detroit and Iowa. Comorbidity is the Klabunde modification of the Charlson Index.[21]
Abbreviation: RT, radiation therapy.

care spending attributable to the increased utilization of these newer modalities.

METHODS

Data Source

Our study was approved by the Brigham and Women's institutional review board and a data-use agreement was in place with the Centers for Medicare and Medicaid Services; patient data were de-identified and the requirement for consent was waived. We used Surveillance, Epidemiology, and End Results (SEER) –Medicare data for analyses, composed of a linkage of population based cancer registry data from 16 SEER areas covering approximately 26% of the US population with Medicare administrative data. The Medicare program provides benefits to 97% of Americans age 65 years or older.[5]

Defining the Study Cohort and Exclusion Criteria

We identified 103,363 men age 65 years or older in the SEER registry with pathologically confirmed prostate cancer from 2002 to 2005, who had no history of other malignancies. We excluded men enrolled in a health maintenance organization or not enrolled in both Medicare Part A and Part B throughout the duration of the study because claims are not reliably submitted for such men. We also excluded men who were missing a date of diagnosis or had metastatic disease. This reduced the cohort to 71,674 men, of which 58,571 men underwent some form of treatment with follow-up through December 31, 2007. The focus of our study was men who underwent surgery or radiation, so we excluded 11,093 men who received primary androgen deprivation therapy and 1,205 who received cryotherapy. We also excluded 619 men who all received proton therapy at a single center because their trends results would not be generalizable. The final study cohort was 45,636 patients.

Determination of Surgery and Radiation Therapies

Treatment type was identified from Medicare inpatient, outpatient, and carrier component files (formerly physician/provider B files) based on the presence of Current Procedural Terminology, Fourth Edition (CPT-4) codes listed in Appendix Table A1 (online only). Brachytherapy and external RT were considered as part of a combination therapy if they were given within 6 months of each other.

Determination of Treatment Cost

To determine the cost of therapy, we summed the total amount paid by Medicare for inpatient, outpatient, and physician services within 12 months of prostate cancer diagnosis.[6] To ensure that we adequately captured the cost of treatment, we included in our cost analysis only men who began treatment within 6 months of the prostate cancer diagnosis. Using each subject as his own control, we subtracted health expenditures accrued in the 12 months before prostate cancer diagnosis, which we considered baseline annual health care costs, from 12-month expenditures after prostate cancer diagnosis.[7] This difference captures the cost of treatment and other services such as preoperative evaluation, imaging, laboratory tests, and treatment of complications within 1 year. The mean cost of each therapy was then tabulated and stratified by the year of diagnosis. All costs were adjusted to 2008 dollars using the 2007 Annual Report of the Boards of Trustees of the Federal Hospital Insurance and Federal Supplementary Medical Insurance Trust Fund Table 5.B.1 HI and SMI Average Per Beneficiary Costs (HI = Part A; SMI = Part B).

Determination of the Excess Direct Medical Spending on More Expensive Therapies at the National Level

To estimate the total amount spent nationwide on more expensive prostate cancer therapies for men of any age, we identified the total number of patients in the US diagnosed with nonmetastatic prostate cancer in 2005 from the SEER limited-use registry treated with surgery, external beam radiation, or brachytherapy plus external beam radiation.[8] We divided these figures by 0.26 to extrapolate national estimates of the number of people receiving each treatment since the SEER registry captures 26% of the US population. We multiplied the number in each treatment category (eg, surgery), by the proportion expected to receive the more expensive therapy to determine the expected number of people receiving the expensive therapy nationwide. The observed rates of utilization found in our cohort were adjusted for demographic differences between the cohort and the US population to develop expected utilization rates applicable to the US population. The number of people receiving each expensive therapy was then multiplied by the mean cost of each therapy to estimate national spending.[9]

Statistical Analyses

Temporal trends in use of the more expensive therapy were examined using the Mantel-Haenszel test for trend. The χ^2 test was used to determine the factors associated with the receipt of the more expensive therapy. A *P* value of lower than .05 was considered statistically significant. We developed directly standardized rates of utilization that would be expected in the general population by weighing each patient in our cohort by the ratio of patients in general population to SEER-Medicare for the strata of demographic characteristics to which each patient belongs.[10] All analyses were performed using SAS version 9.1.3 (SAS Institute Inc, Cary, NC).

RESULTS

Utilization Trends

The characteristics of the study cohort are listed in Table 1, stratified by treatment modality. Of the cohort, 11,894 (26%) received surgery, 17,274 (38%) received external radiation, and 16,468 (36%) received brachytherapy with or without external radiation as their primary therapy (year-by-year analysis in Appendix Table A2, online only). Figures 1A-C demonstrate rapidly increased utilization of the

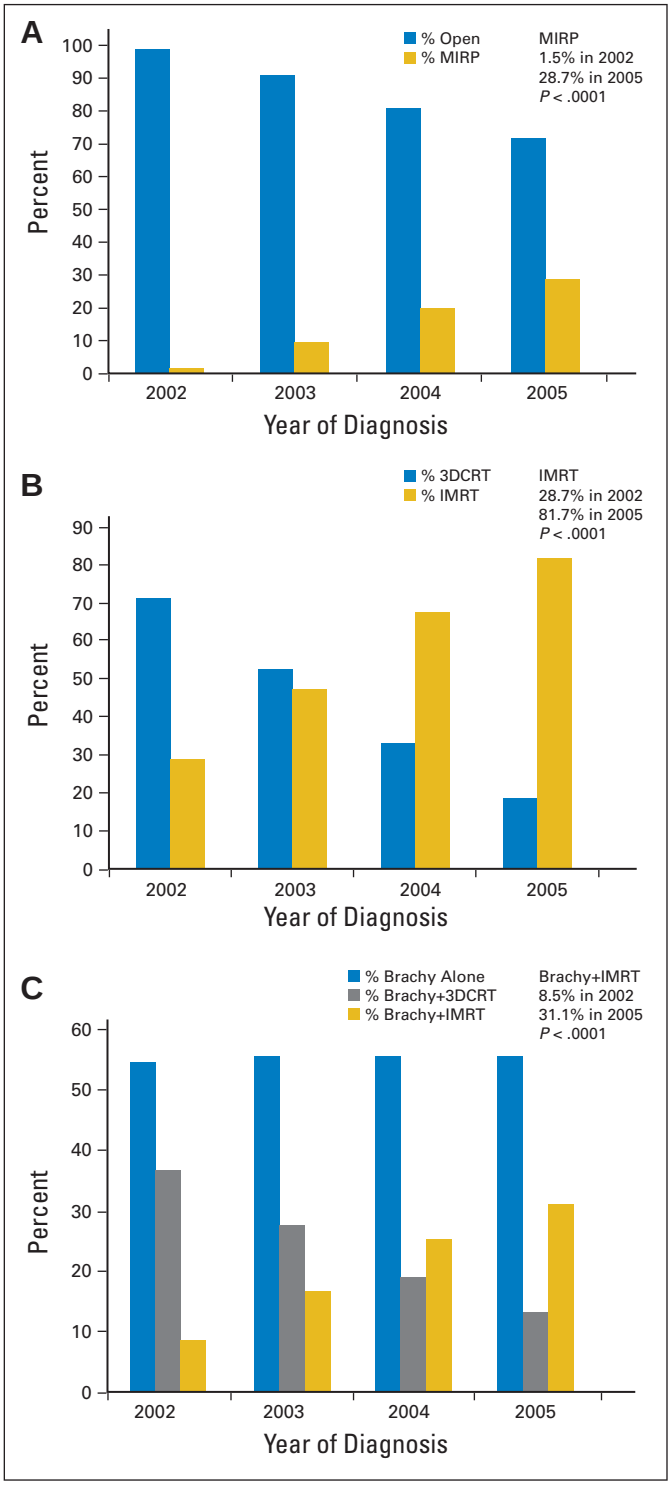

Fig 1. (A) Increasing use of minimally invasive radical prostatectomy (MIRP) among patients receiving surgery. (B) Increasing use of intensity-modulated radiation therapy (IMRT) among patients receiving external radiation. (C) Increasing use of supplemental IMRT among patients receiving brachytherapy (Brachy). 3D-CRT, three-dimensional conformal radiation therapy.

more expensive therapies over the study period. Among men undergoing surgery, MIRP was used by 1.5% of those diagnosed in 2002 versus 28.7% of those diagnosed in 2005 ($P < .001$), while IMRT was used by 28.7% in 2002 versus 81.7% in 2005 ($P < .001$) of those undergoing external radiation, and supplemental IMRT was used for 8.5% in 2002 versus 31.1% in 2005 ($P < .001$) among those receiving brachytherapy. Among just the subgroup of brachytherapy patients receiving supplemental external radiation, supplemental IMRT was used by 18.7% versus 70.2% ($P < .001$). Correspondingly, the use of each of the less expensive therapies (open RP, 3D conformal RT, and brachytherapy plus 3D conformal RT) decreased.

Predictors of Utilization

Table 2 presents a multivariable logistic regression of the factors associated with receiving more expensive therapy. Univariable analysis is listed in Appendix Table A3 (online only). The factors consistently associated with receiving the more expensive therapy regardless of whether they chose surgery or radiation were living in an area with median income $\geq$ $60,000, living in a metropolitan rather than rural area, having T1c disease, and being of Asian descent (all $P < .05$). The pattern of association with other demographic variables was less consistent. In our cohort of patients older than 65 years, the patients older than 75 years made up only 7% of those receiving MIRP, but were 33% of those receiving brachytherapy plus IMRT and 44% of those receiving IMRT. However, age was not a consistent significant predictor of utilization of more expensive therapies.

Cost of Therapy

Table 3 displays the mean cost of each primary therapy in 2008 dollars stratified by their year of diagnosis. Costs for each treatment declined significantly from 2002 to 2005 (all $P \leq .001$). For example, in constant 2008 dollars, IMRT costs fell by 15% from $37,125 to $31,574, brachytherapy plus IMRT costs fell by 16% from $43,723 to $36,795, and MIRP costs fell by 23% from $21,325 (in 2003 since the 2002 estimates are based on small numbers) to $16,469. Nevertheless, newer, more expensive treatments remained costlier than their less expensive alternatives over the study period. Specifically, among men diagnosed in 2005, the mean cost difference between IMRT and 3D-CRT was $10,986. Similarly, the cost difference between brachytherapy plus IMRT and brachytherapy plus 3D-CRT was $10,789, while the cost difference between MIRP and open RP was only $293. In Appendix Table A4 (online only), costs were alternatively estimated by matching controls from the Medicare 5% noncancer sample as outlined by Brown et al.[6]

Estimate of Excess Direct Medical Spending on Costlier Therapies at the National Level

Compared to the less costly alternative, the nationwide excess direct spending (Table 4) for the rapid adoption of more expensive therapies was $282 million for IMRT, $59 million for brachytherapy plus IMRT, and $4 million for MIRP for men diagnosed in 2005 (assuming that all treatments were reimbursed at Medicare rates).

DISCUSSION

Our study has several important findings. First, we found a rapid and substantial increase in the utilization of MIRP, IMRT, and brachytherapy plus IMRT, which are more expensive alternatives to traditional open RP, 3D-CRT, and brachytherapy plus 3D-CRT, respectively. Men who received the more expensive therapies tended to reside in wealthier areas, and in metropolitan as opposed to rural areas, possibly

Table 2. Multivariable Logistic Analysis of Factors Associated With More Expensive Therapy

Variable	MIRP *v* Open RP			IMRT *v* 3DCRT			Brachy/IMRT *v* Brachy/3DCRT		
	OR	95%CI	*P*	OR	95%CI	*P*	OR	95%CI	*P*
Outcome	MIRP			IMRT			Brachy/IMRT		
Age at diagnosis, years									
65-69	1.09	0.88 to 1.36	.4204	**1.18**	**1.09 to 1.28**	**< .001**	0.96	0.84 to 1.08	.4813
70-74	1.1	0.87 to 1.38	.4312	1.05	0.98 to 1.13	.1522	1.03	0.91 to 1.16	.6409
75+	1.00		ref	1.00		ref	1.00		ref
Comorbidity									
0	1.1	0.82 to 1.48	.5253	**1.14**	**1.03 to 1.26**	**.0135**	0.97	0.81 to 1.17	.7458
1	0.96	0.7 to 1.33	.8258	1.01	0.9 to 1.13	.876	0.99	0.81 to 1.21	.9107
2+	1.00		ref	1.00		ref	1.00		ref
Race									
White/Non-Hispanic	1.00		ref	1.00		ref	1.00		ref
Black/Non-Hispanic	0.91	0.71 to 1.15	.4284	**1.18**	**1.06 to 1.33**	**.0034**	1.17	0.99 to 1.38	.0608
Hispanic	**0.74**	**0.57 to 0.98**	**.0342**	**1.16**	**1 to 1.35**	**.0461**	**1.33**	**1.06 to 1.66**	**.0121**
Asian/Non-Hispanic	**1.51**	**1.18 to 1.93**	**.0011**	**1.49**	**1.27 to 1.76**	**< .001**	**1.43**	**1.11 to 1.86**	**.0062**
Other/unknown	1.03	0.65 to 1.66	.8868	1.21	0.97 to 1.51	.0894	1.27	0.84 to 1.93	.2561
High school education in patient's census region, %									
< 75	1.00		ref	1.00		ref	1.00		ref
75-84.99	0.99	0.8 to 1.22	.9448	**1.24**	**1.12 to 1.38**	**< .001**	1.06	0.9 to 1.25	.4966
85-89.99	**0.79**	**0.62 to 0.99**	**.0402**	**1.3**	**1.16 to 1.46**	**< .001**	**1.25**	**1.04 to 1.51**	**.0176**
90+	**0.74**	**0.58 to 0.93**	**.0111**	**1.52**	**1.35 to 1.73**	**< .001**	1.15	0.95 to 1.4	.1619
Median income, $									
< 35,000	1.00		ref	1.00		ref	1.00		ref
35,000-44,999	**1.49**	**1.24 to 1.79**	**< .001**	1.02	0.93 to 1.12	.6857	0.99	0.85 to 1.15	.8532
45,000-59,999	**1.91**	**1.57 to 2.33**	**< .001**	**1.13**	**1.02 to 1.26**	**.0228**	0.99	0.83 to 1.17	.8912
≥ 60,000	**3.1**	**2.49 to 3.85**	**< .001**	**1.47**	**1.29 to 1.67**	**< .001**	**1.31**	**1.07 to 1.59**	**.0075**
Region									
West	1.00		ref	1.00		ref	1.00		ref
Northeast	0.95	0.8 to 1.12	.5351	1.03	0.95 to 1.12	.4834	**2.17**	**1.91 to 2.47**	**< .001**
South	**0.73**	**0.61 to 0.88**	**.0009**	**0.74**	**0.67 to 0.82**	**< .001**	**1.65**	**1.43 to 1.91**	**< .001**
Midwest	**1.39**	**1.19 to 1.63**	**< .001**	**0.64**	**0.58 to 0.7**	**< .001**	**0.57**	**0.47 to 0.7**	**< .001**
Marital status									
Unmarried	1.00		ref	1.00		ref	1.00		ref
Married	0.99	0.84 to 1.16	.8818	1.04	0.96 to 1.12	.3355	1	0.88 to 1.13	.9599
Unknown	2.37	1.86 to 3.04	< .001	1.17	1.03 to 1.32	.0132	1.92	1.54 to 2.4	< .001
Population density									
Metropolitan	1.00		ref	1.00		ref	1.00		ref
Nonmetropolitan county	**0.75**	**0.58 to 0.97**	**.0307**	**0.76**	**0.67 to 0.85**	**< .001**	**0.52**	**0.41 to 0.66**	**< .001**
Grade/differentiation									
Well	1.00		ref	1.00		ref	1.00		ref
Moderately	1.09	0.62 to 1.93	.7538	1.13	0.86 to 1.49	.3752	0.86	0.5 to 1.46	.5726
Poorly	1.58	0.9 to 2.78	.1149	**1.73**	**1.32 to 2.28**	**< .001**	1.1	0.65 to 1.88	.7175
Unknown/missing	1.26	0.51 to 3.13	.6222	0.96	0.67 to 1.38	.8371	0.73	0.38 to 1.38	.3313
Clinical stage									
T1	1.00		ref	1.00		ref	1.00		ref
T2	**0.61**	**0.54 to 0.68**	**< .001**	**0.71**	**0.66 to 0.76**	**< .001**	**0.63**	**0.57 to 0.7**	**< .001**
T3	**0.53**	**0.33 to 0.86**	**.0104**	**0.67**	**0.57 to 0.8**	**< .001**	**0.71**	**0.53 to 0.94**	**.0169**
T4	0.36	0.08 to 1.62	.1853	**0.45**	**0.32 to 0.65**	**< .001**	0.71	0.23 to 2.23	.5637
Unknown/missing	0.29	0.15 to 0.56	.0002	0.72	0.58 to 0.9	.0038	0.8	0.51 to 1.25	.3183

NOTE. Boldface indicates statistical significance.
Abbreviations: MIRP, minimally invasive radical prostatectomy; Open RP, open radical prostatectomy; IMRT, intensity-modulated radiation therapy; 3DCRT, three-dimensional conformal radiation therapy; Brachy, brachytherapy; ref, referent.

due to the greater availability of newer technologies in these locations or greater marketing efforts directed toward their inhabitants. Of note, Asian race was consistently associated with 1.5-fold odds of receiving a more expensive therapy compared with white race, but the underlying reasons for this could not be determined from this study. Men undergoing the more expensive therapies also tended to have lower stage disease, which may reflect increased screening in more affluent populations, or perhaps a provider bias of offering these therapies to patients who will likely be cured of their prostate cancer and thereby have more time to benefit from any perceived reduction in long-term toxicity.

There are no randomized trials assessing whether newer treatments such as MIRP or IMRT have any clinical benefit over their less-expensive counterparts; the only available data currently come

Table 3. Mean Cost of Each Primary Therapy Among Medicare Enrollees, Stratified by Year of Diagnosis

	$						
Year	3DCRT	IMRT	Brachy	Brachy+ 3DCRT	Brachy+ IMRT	Open RP	MIRP
2002	22,384	37,125	21,117	28,770	43,723	18,070	29,988
2003	23,542	37,418	19,476	27,320	43,364	17,423	21,325
2004	22,023	33,237	18,308	26,756	39,453	16,930	17,645
2005	20,588	31,574	17,076	26,006	36,795	16,469	16,762
P trend	< .001	< .001	< .001	< .001	< .001	< .001	.001

Abbreviations: 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; Brachy, brachytherapy; Open RP, open radical prostatectomy; MIRP, minimally invasive radical prostatectomy.

from retrospective studies. For instance, an observational, population-based study comparing outcomes after MIRP versus open RP found that MIRP appeared to be associated with a shorter length of stay (2 *v* 3 days), fewer transfusions (2.7% *v* 20.8%), fewer postoperative respiratory complications (4.3% *v* 6.6%), and fewer anastomotic strictures (5.8% *v* 14.0%). However, MIRP was also associated with an increased risk of genitourinary complications (4.7% *v* 2.1%) and diagnoses of incontinence (15.9 per *v* 12.2 per 100 person-years) and erectile dysfunction (26.8 *v* 19.2 per 100 person-years).[11] For external radiation, retrospective studies seem to consistently suggest that IMRT is associated with a significant reduction in long-term rectal bleeding compared to 3D-CRT. Zelefsky et al demonstrated that men treated to 81 Gy with IMRT versus conformal radiation experienced a significantly lower risk of ≥ grade 2 rectal bleeding, (2% *v* 14%, respectively), and other retrospective series have had similar findings.[12-14]

However, even if there is some underlying clinical benefit to these newer more expensive therapies, it is still important to ask whether the marginal benefit of these therapies is large enough to justify their higher cost.

We found that the rapid shift to more expensive therapies versus less costly counterparts resulted in a national cost burden of more than $350 million among patients diagnosed in 2005. Specifically, Medicare expenditures for IMRT were nearly $11,000 greater per case compared to 3D-CRT and were also nearly $11,000 greater per case for brachytherapy plus IMRT compared to brachytherapy plus 3D-CRT. While the Medicare expenditures for MIRP appeared to be only $236 more per case than for open radical prostatectomy, this surgical amount only approximates the difference in Medicare reimbursed surgeon fees between MIRP and open RP, and does not nearly reflect the full extent of the underlying cost difference between the surgical procedures. For instance, the most widespread form of MIRP presently is

Table 4. Estimates of Additional Direct Costs As a Result of Newer Technologies

	MIRP *v* Open RP						
Year	Utilization of MIRP From Our Cohort	Weighted Estimated Utilization of MIRP in US	Total No. in SEER Who Underwent Surgery	Estimated Total No. in the US Who Underwent Surgery	Estimated No. of MIRP in the US	Mean Cost Difference Between MIRP and Open RP ($)	Total Cost Savings If All MIRP in US Changed to Open RP ($)
2002	1.49	1.14	15,368	59,108	674	11,918	8,030,720
2003	9.48	7.78	14,760	56,769	4,417	3,902	17,233,683
2004	19.59	18.17	15,360	59,077	10,734	715	7,675,018
2005	28.66	25.17	13,866	53,331	13,423	293	**3,933,060**
	IMRT *v* 3D-CRT						
Year	Utilization of IMRT From Our Cohort	Weighted Estimated Utilization of IMRT in US	Total No. in SEER Who Underwent RT	Estimated Total No. in the US Who Underwent RT	Estimated No. of IMRT in the US	Mean Cost Difference Between IMRT and 3DCRT ($)	Total Saving Cost If All IMRT in US Changed to 3DCRT ($)
2002	28.65	23.35	10,656	40,985	9,570	14,741	141,071,333
2003	47.20	39.62	10,148	39,031	15,464	13,876	214,579,605
2004	67.31	58.80	10,006	38,485	22,629	11,214	253,763,625
2005	81.66	74.18	8990	34,577	25,649	10,986	**281,782,316**
	Brachy/IMRT *v* Brachy/3D-CRT						
Year	Utilization of Brachy/IMRT From Our Cohort	Weighted Estimated Utilization of Brachy/IMRT in US	Total No. in SEER Who Underwent Brachy + RT	Estimated Total No. in the US Who Underwent Brachy + RT	Estimated No. of Brachy/IMRT in the US	Mean Cost Difference Between Brachy/IMRT and Brachy/EBRT ($)	Total Cost Savings If All Brachy/IMRT in US Changed to Brachy/EBRT ($)
2002	18.66	15.51	2,914	11,208	1,738	14,953	25,993,709
2003	37.54	36.49	2,136	8,215	2,998	16,044	48,094,353
2004	57.26	53.72	1,931	7,427	3,990	12,697	50,658,293
2005	70.19	71.27	2,000	7,692	5,482	10,789	**59,146,252**

Abbreviations: MIRP, minimally invasive radical prostatectomy; Open RP, open radical prostatectomy; SEER, Surveillance, Epidemiology, and End Results database; IMRT, intensity-modulated radiation therapy; Brachy, brachytherapy; 3DCRT, three-dimensional conformal radiation therapy.

robotic-assisted prostatectomy, which requires at least a $1.4 million upfront investment to purchase the robot and then a $140,000 annual maintenance for the robot.[3] Importantly, while private health plans may reimburse a facility fee, Medicare does not reimburse for the use of the robot. Therefore, this fixed component of the costs cannot be accounted for by a Medicare claims–based analysis, which makes the cost difference between open RP and MIRP seem artificially small. Moreover, our Medicare-based cost estimates likely underestimate the true expense of the rapid shift to newer, more costly technologies, as Medicare typically reimburses a lower amount compared to private health plans.

Just as the newer technologies have been widely adopted without rigorous efficacy trials, they have also been adopted without robust cost-effectiveness analysis. To our knowledge, there are no data on the cost-effectiveness of MIRP. As for the cost-effectiveness of IMRT, a study by Konski et al suggested that based on its likely reduction in rectal toxicity, IMRTs incremental cost per quality-adjusted life year was $40,101, which meets the typical requirement that treatments have an incremental cost/quality-adjusted life year lower than $50,000 to be considered cost-effective.[15] However, that article was not published until 2006, and this study suggests that by then, 81% of external radiation patients were already receiving IMRT, making it likely that even if IMRT were found to not be cost effective, it would have been nearly impossible to reverse the nationwide trend in its use.

This research has implications for predicting the patterns of use of other newer and more expensive technologies in health care, as these trends are likely not unique to prostate cancer. It suggests that when a newer expensive technology becomes available and is reimbursed by health plans, it is likely to be rapidly adopted even before there is adequate data on its clinical benefits and cost effectiveness. This study may also inform the debate about the use of proton therapy for prostate cancer. Proton therapy carries a significantly higher price tag than IMRT, with some estimates showing it is about twice as expensive.[16] There are also significant marketing efforts promoting protons for prostate cancer and growing patient interest in receiving it. While protons are likely less toxic for certain pediatric and CNS tumors,[17,18] it remains unknown whether protons for prostate cancer are superior to IMRT in terms of cancer control or toxicity, and there is great uncertainty about whether proton therapy for prostate cancer could be cost-effective.[16,19] Nevertheless, if protons become more widely available, the trends seen in the rapid uptake of IMRT for prostate cancer may well be repeated with proton therapy.

Proponents of allowing the widespread adoption of higher-cost therapies before they are proven may point out that as a technology becomes more widely used, its costs will decrease over time. This is in fact reflected in Table 3, which shows the mean cost of IMRT falling by 20% from 2002 to 2005, and of MIRP falling by 12% over the same time period. These drops in the inflation-adjusted cost of each prostate cancer therapy are corroborated by other reports.[7] As the prices of these newer technologies falls, the likelihood that they will become cost effective can theoretically increase. However, it should be noted that the costs of the less-expensive therapies were also falling over that same time period. If the cost of the less expensive therapy is also falling, then the more expensive therapy may remain equally cost-ineffective despite its lower absolute price tag.

This study has certain limitations. First, we may have overestimated the excess costs of the new therapies because we could only look at direct Medicare costs, and could not factor in the potential indirect cost benefits, such as MIRP potentially leading to fewer missed working days for patients. In addition, our 12-month cost methodology cannot capture potential long-term savings from toxicity reduction, such as IMRT potentially reducing the need for late interventions for rectal bleeding. We also could not account for any potential long-term savings that could be due to higher cure rates and lower need for salvage therapies. Also, as more surgeons performing MIRP overcome their learning curves, the cost differentials between MIRP and open RP may fall. Conversely, we may have underestimated the excess costs because to be consistent with other cost studies we only accounted for direct Medicare payments and excluded payments made by beneficiaries and supplemental insurance. Accounting for these additional payments would have increased our estimated excess expenditures by approximately 30%. Finally, as mentioned above, the cost estimates were entirely based on patients enrolled in Medicare, and applying the mean Medicare costs to younger patients who may have private insurance that reimburses at higher rates likely leads to an underestimate of the true nationwide expenditures on the more expensive therapies.

Despite limited comparative effectiveness research, newer and costlier prostate cancer therapies were rapidly and widely adopted, resulting in an excess national spending of more than $350 million among men diagnosed in 2005. This pattern of rapid adoption may provide some empirical evidence for why health care costs account for 17% of the US gross domestic product,[20] and suggests the need for increased comparative effectiveness research to accurately weigh costs and benefits.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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Overuse of Imaging for Staging Low Risk Prostate Cancer

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Purpose: Routine imaging for staging low risk prostate cancer is not recommended according to current guidelines. We characterized patterns of care and factors associated with imaging overuse.

Materials and Methods: We used SEER-Medicare linked data to identify men diagnosed with low risk prostate cancer from 2004 to 2005, and determined if imaging (computerized tomography, magnetic resonance imaging, bone scan, abdominal ultrasound) was obtained following prostate cancer diagnosis before treatment.

Results: Of the 6,444 men identified with low risk disease 2,330 (36.2%) underwent imaging studies. Of these men 1,512 (23.5%), 1,710 (26.5%) and 118 (1.8%) underwent cross-sectional imaging (computerized tomography or magnetic resonance imaging), bone scan and abdominal ultrasound, respectively. Radiation therapy vs surgery was associated with greater odds of imaging (OR 1.99, 95% CI 1.68–2.35, p <0.01), while active surveillance vs surgery was associated with lower odds of imaging (OR 0.44, 95% CI 0.34–0.56, p <0.01). Associated with increased odds of imaging was median household income greater than $60,000 (OR 1.41, 95% CI 1.11–1.79, p <0.01), and men from New Jersey vs San Francisco (OR 3.11, 95% CI 2.24–4.33, p <0.01) experienced greater odds of imaging. Men living in areas with greater than 90% vs less than 75% high school education experienced lower odds of imaging (OR 0.76, 95% CI 0.6–0.95, p = 0.02).

Conclusions: There is widespread overuse and significant geographic variation in the use of imaging to stage low risk prostate cancer. Moreover treatment associated variation in imaging was noted with the greatest vs lowest imaging use observed for radiation therapy vs active surveillance.

Key Words: diagnostic imaging, health services misuse, prostatic neoplasms, health expenditures

Abbreviations and Acronyms

ACR = American College of Radiologists
CT = computerized tomography
MRI = magnetic resonance imaging
NCCN = National Comprehensive Cancer Network
PSA = prostate specific antigen
SEER = Surveillance, Epidemiology and End Results

PROSTATE cancer remains the most commonly diagnosed solid organ tumor among United States men with approximately 192,280 incident cases in 2009.[1] Due to widespread PSA screening and resultant stage migration, the majority of men are diagnosed with low risk disease as defined by D'Amico et al as clinical stage T1c or T2a, PSA less than 10 ng/ml and Gleason score less than or equal to 6.[2] While the appropriate treatment for men with these indolent tumor characteristics is widely debated, the risk of metastasis is low, obviating the need for imaging for staging purposes. Because there is a less than 1% chance of a positive bone scan or CT when imaging men with low risk prostate cancer,[3–8] the ACR[9] and the

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NCCN[10] advised against routine imaging for men with low risk features.

Despite the recommendations of the ACR and NCCN, Plawker et al found that 28.6% and 52.4% of urologists in 1997 ordered CT and bone scan, respectively, for all men with prostate cancer regardless of risk.[11] Using data from an observational cohort of men with prostate cancer Cooperberg et al reported persistent inappropriate use with 22.7% of men diagnosed with low risk prostate cancer undergoing radiographic staging before treatment.[12]

More recently emerging evidence has shown that the overall use of imaging, especially CT, is increasing, and that there is widespread variation in use and cost without apparent benefit.[13] Against this backdrop we characterized patterns of care and factors associated with the use of imaging in men with low risk prostate cancer using a contemporary, population based, observational cohort.

MATERIALS AND METHODS

Data

Our study was approved by the Brigham and Women's institutional review board. Patient data were de-identified and the requirement for consent was waived. We used SEER-Medicare[14] data for analysis, which is comprised of a linkage of population based cancer registry data from 16 SEER areas with Medicare administrative data, and covers approximately 26% of the United States population. The Medicare program provides benefits to 97% of Americans 65 years old or older.[15]

Study Cohort

We identified 49,364 men 65 years old or older diagnosed with prostate cancer during 2004 to 2005 with at least 1 year of followup after diagnosis to ascertain whether imaging was obtained and the type of treatment rendered. We excluded from study 5,404 men who were enrolled in a health maintenance organization or who were not enrolled in Medicare Part A and Part B because claims are not reliably submitted for these men. To increase sensitivity for detection of imaging we restricted our analyses to men with prostate cancer as their first and only cancer, and excluded 3,378 men with other cancers including nonmelanoma skin cancers. We also excluded 8,249 men diagnosed with metastatic prostate cancer. Finally, we excluded men with intermediate (14,884), high (7,388) and unknown (3,617) risk disease, which provided our cohort with 6,444 men with low risk prostate cancer.[2] Demographic and tumor characteristics were obtained from SEER registry data while patient age was obtained from the Medicare file. Comorbidity was assessed using the Klabunde modification of the Charlson index based on claims submitted during the year before surgery.[16] The Klabunde modification uses comorbid conditions identified by the Charlson comorbidity index, and incorporates the diagnostic and procedure data contained in Medicare physician (Part B) claims.

Outcomes

We examined the use of pretreatment imaging after prostate cancer diagnosis for low risk prostate cancer. These imaging modalities included cross-sectional imaging (CT, MRI, endorectal coil MRI), bone scan and abdominal ultrasound. Cross-sectional imaging for radiation treatment planning was excluded from analysis because this is billed with unique CPT-4 codes. We included only imaging studies designated with a corresponding primary ICD-9 diagnosis code 185.0 for prostate cancer.

Treatments

Treatment choice was determined by the corresponding CPT-4 and ICD-9 codes from Medicare inpatient, outpatient and carrier component files (formerly Physician/Provider B files). Surgical therapy included open radical prostatectomy, open perineal prostatectomy and minimally invasive radical prostatectomy. Radiation therapy included brachytherapy, brachytherapy combined with 3-dimensional conformal external beam radiation therapy or intensity modulated radiation therapy, external beam radiation therapy alone, intensity modulated radiation therapy alone, and proton beam therapy. Men undergoing hormone ablation were identified based on the presence of the Healthcare Common Procedure Coding System codes used for gonadotropin-releasing hormone agonists without a designation for definitive therapy. Men avoiding definitive therapy for 12 or more months after diagnosis were categorized as on active surveillance.

Statistical Analysis

Characteristics associated with over-imaging for low risk disease were compared with the Pearson chi-square statistic and the Fisher exact test. Univariable and multivariable logistic regression analyses were performed to identify clinical covariates significantly associated with an increased likelihood of having imaging.[17] A multivariate logistic regression model was constructed with year of diagnosis, age, Charlson comorbidity index, race, marital status, education level, income, SEER region, population density (urban vs rural) and treatment type as covariates. All tests were considered statistically significant at $\alpha = 0.05$. Analyses were performed with SAS® version 9.2.

RESULTS

The demographics of our study population are summarized elsewhere. We observed an increased use of imaging among men treated with radiation followed by surgery and active surveillance (45.5%, 26.1% and 12.8%, $p < 0.01$). Moreover while age, race, marital status, year of diagnosis and comorbidity were not associated with imaging use, there was significant geographic variation in the use of imaging with New Jersey vs Seattle having the highest and lowest use rates (61.6% vs 18.0%, $p < 0.01$). Men with median household incomes greater than $60,000 vs less than $35,000 were more likely to undergo imaging (39.6% vs 35.6%, $p = 0.03$), while men living in areas with 90% or greater vs less than 75% high school

education were less likely to undergo imaging (33.7% vs 37.4%, p = 0.01).

Results from adjusted analysis were consistent with these results. Median household incomes greater than $60,000 vs less than $35,000 experienced greater odds of imaging (OR 1.41, 95% CI 1.11–1.79, p <0.01), while men living in areas with greater than 90% vs less than 75% high school education experienced lower odds of imaging (OR 0.76, 95% CI 0.6–0.95, p = 0.02). Men living in New Jersey (OR 3.11, 95% CI 2.24–4.33, p <0.01), Hawaii (OR 1.84, 95% CI 1.22–2.79, p <0.01) and Los Angeles (OR 1.68, 95% CI 1.18 – 2.41, p <0.01) experienced greater odds of imaging compared to San Francisco, while men living in Seattle experienced lower odds of imaging (OR 0.6, 95% CI 0.40–0.91, p = 0.02). Finally, men undergoing radiation (OR 1.99, 95% CI 1.68–2.35, p <0.01) vs surgery experienced greater odds of imaging, while those undergoing active surveillance (OR 0.44, 95% CI 0.34–0.56, p <0.01) vs surgery experienced lower odds of imaging. Finally, the use of imaging did not differ significantly for cryotherapy and hormone therapy compared to surgery.

The type of imaging obtained by treatment type is shown in the table. Overall 36.2% of men underwent at least 1 imaging study before treatment. Cross-sectional imaging was performed in 23.5% of men while 26.5% underwent a bone scan. Additionally, 1.8% of men underwent abdominal ultrasound. Moreover 3,340 imaging studies were performed in 2,330 men, and men undergoing imaging received 1.4 studies on average. Men undergoing radiation therapy vs surgery were more likely to receive cross-sectional imaging (31.5% vs 15.9%, p <0.01) and bone scans (32.9% vs 21.4%, p <0.01). Of note, CT comprised more than 97% of all cross-sectional imaging studies obtained.

DISCUSSION

With the widespread use of PSA screening there has been greater detection of low risk prostate cancer.[2] Prior studies have demonstrated the rarity of positive radiographic findings when imaging men with low risk features[3–8] and current guidelines do not recommend imaging for low risk disease.[9,10] Hunchrarek and Muscat estimated that eliminating unnecessary CTs alone may net a cost savings of $20 to $50 million a year in direct prostate cancer expenditures.[18] Although the exact cost burden (direct and indirect) of the overuse of imaging remains unknown, it is likely high given the large number of men exposed. Assuming 232,090 men were diagnosed with prostate cancer in 2005[19] and half were diagnosed with low risk disease, extrapolating from our findings suggests that at least 41,000 men were exposed to 58,800 studies that year.

Our study has several important findings. There is widespread overuse of imaging for low risk prostate cancer. We found that more than a third of men with low risk disease underwent imaging before treatment. We limited our analysis to those men with low risk disease because there is clear consensus that these men should not undergo imaging. Oesterling studied 2,064 consecutive men with prostate cancer and a PSA less than 20 ng/ml, and found 7 (0.3%) had a positive bone scan with only 1 positive finding with a PSA less than 10 ng/ml.[4] In a study of 861 men with prostate cancer Levran et al found that 13 (1.5%) had nodal disease on CT confirmed by biopsy and that all of these men had a PSA greater than 20 ng/ml.[6] In addition, no positive bone scans were found in men with PSA less than 20 ng/ml. Similarly Lee et al studied 588 men with low risk prostate cancer and did not identify a positive CT among them.[7] In a recent review of MRI and functional MRI techniques used in prostate cancer Seitz et al found functional MRI more reliable than conventional MRI in detecting and staging prostate cancer.[20] However, there are currently no guidelines available to suggest which technique is optimal in a specific clinical scenario. Interestingly there is improved accuracy when combining the Kattan nomogram variables with MRI/magnetic resonance spectroscopy.[21] However, MRI detection of extracapsular extension varies widely, ranging from 54% to 83%, with improved accuracy when MRI is combined with functional MRI.[20] These studies led the NCCN and

Type of imaging ordered and treatment rendered

	Watchful Waiting	Hormone Ablation Only	Surgery	Cryotherapy	Radiation	Totals
No. men treated	1,096	273	1,026	116	3,933	6,444
No. men with imaging (%)	140 (12.8)	95 (34.8)	268 (26.1)	37 (31.9)	1,790 (45.5)	2,330 (36.2)
No. cross-sectional (%)*	44 (4.0)	47 (17.2)	163 (15.9)	23 (19.8)	1,235 (31.5)	1,512 (23.5)
No. bone scan (%)	91 (8.3)	84 (30.8)	220 (21.4)	23 (19.8)	1,292 (32.9)	1,710 (26.5)
No. abdominal ultrasound (%)	Less than 11 (less than 1)†	Less than 11 (less than 4)†	22 (2.1)	Less than 11 (less than 9)†	83 (2.1)	118 (1.8)

All values p < 0.01.

* Includes CT and MRI.

† Values less than 11 censored for confidentiality.

the ACR to advise against the routine use of pretreatment imaging for low risk disease.[9,10] Recently Briganti et al validated the existing guidelines for bone scan use, finding them to be highly accurate.[22] Furthermore, the use of bone scans in men with low risk prostate cancer is a negative quality indicator in the Physician Performance Measurement Set for Prostate Cancer, which was proposed for implementation in the 2008 Physician Quality Reporting Initiative.[23] The Physician Quality Reporting Initiative is a Centers for Medicare and Medicaid Services initiative linking physician reimbursement to quality. While the use of abdominal ultrasound in our series for staging purposes is uncommon, it is unwarranted for staging purposes.

In addition, we found significant variation in treatment rendered and in demographics in the use of pretreatment imaging. In adjusted analyses while the likelihood of imaging for men undergoing surgery vs hormone ablation vs cryotherapy was similar, the likelihood of imaging for men undergoing radiation vs surgery was 2-fold greater. These results are similar to those of other studies that adjusted for age and comorbidities, and demonstrated that men were more likely to undergo radiographic staging before radiation therapy vs surgery.[24] Differences in practice patterns across specialties and access to imaging modalities may contribute to this finding. Additionally, men on active surveillance vs those treated with surgery were less likely to undergo radiographic imaging.

We also found significant geographic variation in use. For instance, men in New Jersey were 5 times more likely to undergo imaging than those in Seattle. These results are consistent with previous reports showing significant geographic variability. In 2000 Albertsen et al showed that rates of CT in pretreatment imaging for all risks of prostate cancer varied from 83% in Connecticut to 58% in Seattle.[25] Similarly in 2002 Cooperberg et al showed that men living in the East had a higher chance of undergoing imaging (75.4%) vs those living in the West (52.1%).[26] While other studies have shown that insurance type was predictive of test use in men with prostate cancer,[11,26] we observed a striking geographic variation in our study of Medicare beneficiaries.

Finally, men living in areas of greater income were more likely to undergo imaging for low risk disease. This may be a result of increased patient demand and better access to imaging modalities. Men living in areas of greater income may be more likely to expect imaging for staging purposes,[27] may possess generous supplemental insurance, and may be more likely to afford copayments and, therefore, more likely to access imaging. However, men residing in areas of greater education were less likely to receive over-imaging. We performed a subanalysis demonstrating that only 43% of men living in areas with greater than 90% high school education lived in areas where the median income was greater than $60,000, allowing for the duality of these findings. Ultimately men living in areas or physicians treating men living in areas with more than a 90% high school education rate may better understand the low yield and extraneous cost of pretreatment imaging for low risk prostate cancer.

Variation in prostate cancer health delivery is not limited to radiographic staging. The Dartmouth Atlas of Healthcare Project found that radical prostatectomy was characterized by the greatest local variation of all the procedures studied. The absolute rate of radical prostatectomy, adjusted for prostate cancer prevalence, varied by almost 10-fold from region to region.[28] Moreover Fisher et al demonstrated wide geographic variation in total Medicare costs, in part driven by the use of diagnostic tests, but no difference in access to or quality of care.[29]

Our study must be interpreted in the context of the study design. Administrative data are primarily designed to provide billing information, not detailed clinical information. The SEER-Medicare data linkage was initiated to examine population based patterns of care.[14] Our findings may not be generalizable to men younger than 65 years. However, previous studies have shown that age does not predict test use before treatment in men with prostate cancer.[26] Finally, our measures of use may overestimate radiographic staging for low risk disease. However, we excluded men with other malignancies from our cohort and only included imaging studies performed with a primary diagnosis of prostate cancer. Furthermore, approximately 70% of our study population had no comorbidities while approximately 20% had a Charlson comorbidity index of 1, reducing the likelihood of nonprostate cancer imaging studies. Moreover the number and severity of comorbidities were not significantly associated with the use of pretreatment imaging.

In summary, treatment type, geographic variation, and patient income and education contributed to 36% of men with low risk prostate cancer undergoing unnecessary pretreatment imaging for staging purposes despite existing expert guidelines. Dunnick et al surmised that inappropriate use of imaging studies was a result of physician ignorance, patient expectations, defensive medicine and economic gain from self-referral.[27] This is particularly relevant for men with low risk disease because prostate cancer has been called a litmus test for health care reform with costly treatments and mediocre results.[30]

CONCLUSIONS

There is significant geographic variation and overuse of imaging for low risk prostate cancer, particularly for men of greater income, living in areas of lesser education, and for those undergoing radiation therapy.

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BJUI BJU INTERNATIONAL

Trends in the care of radical prostatectomy in the United States from 2003 to 2006

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Study Type – Therapy (outcomes research)
Level of Evidence 2b

What's known on the subject? and What does the study add?
There is an increasing trend of minimally invasive treatments for prostate cancer with increased utilization of robotic technology contributing largely to this trend. Our study found that increased utilization of MIRP corresponded with a decreasing trend for complications, blood transfusions, lengths of stay and need for reoperation. Additionally, MIRP was found to have fewer associated complications compared with men undergoing open procedures.

OBJECTIVE

- To determine differences in surgical outcomes by surgical approach during a period of rapid adoption of minimally invasive surgical approaches in radical prostatectomy.

PATIENTS AND METHODS

- We identified 19 542 men undergoing minimally invasive (MIRP), perineal (PRP), and retropubic (RRP) radical prostatectomy from 2003 to 2006 from the MarketScan® Medstat database, a national employer-based administrative database.
- We assessed for temporal trends in perioperative complications, use of postoperative cystography and anastomotic strictures by surgical approach.

RESULTS

- Between 2003 and 2006, MIRP use increased 33.6% vs 31.8% and 1.7% decreases in RRP and PRP, respectively. During the 4-year study, median length of stay for MIRP decreased from 2.0 to 1.0 day ($P = 0.004$) and overall perioperative complications decreased from 13.8 to 10.7%, ($P = 0.023$).
- These findings were driven by reductions in genitourinary complications (3.3 to 2.5%, $P = 0.049$), miscellaneous surgical complications (3.6 to 2.3%, $P = 0.006$) and intestinal injury (1.5 to 0.1%, $P = 0.009$).
- Median length of stay for RRP decreased from 3.2 to 2.9 days, ($P < 0.001$), overall perioperative complications decreased from 18.1 to 14.6%, ($P = 0.007$), because of reductions in both wound/bleeding complications (2.0 to 1.1%, $P = 0.002$) and heterologous blood transfusions.
- Men undergoing MIRP vs RRP were less likely to have perioperative complications (12.5 vs 17.1%, $P < 0.001$), blood transfusions (1.5 vs 8.9%, $P < 0.001$) and anastomotic strictures (6.3 vs 12.8%, $P < 0.001$), and they had shorter mean lengths of stay (1.8 vs 3.1 days, $P < 0.001$) during the study period.

CONCLUSION

- The increased use of MIRP corresponds with a decreasing trend for complications, blood transfusions, lengths of stay and need for reoperation. Additionally, MIRP was found to have fewer associated complications compared with men undergoing open procedures. Further study is needed to assess the impact of tumour characteristics and surgeon volume on these perioperative outcomes as well as effects on long-term cancer control.

KEYWORDS

complications, prostate cancer, radical prostatectomy minimally invasive

INTRODUCTION

After the application of robotic assistance to laparoscopic approaches to radical prostatectomy in 2000, the utilization rate of minimally invasive radical prostatectomy (MIRP) has surged in the USA. However, comparative effectiveness studies of surgical outcomes and associated complications of the competing surgical approaches remains sparse [1].

The use of nerve-sparing approaches in radical prostatectomy has improved postoperative morbidity and with their dissemination over the past 20 years there has been a decrease in retropubic radical prostatectomy (RRP) postoperative morbidity. Although MIRP has not had a similar period to refine surgical technique, the intrinsic advantages of robotic assistance (magnification, motion scaling and tremor filtration) arguably provide potentially superior technical reconstruction of the urethrovesical anastomosis and nerve-sparing and subsequently improve perioperative and postoperative outcomes. The two approaches

have been previously compared in single institution settings but we sought to assess this hypothesis by evaluating temporal trends between the varying surgical approaches nationally in a community setting.

PATIENTS AND METHODS

We identified a population of 19 542 men with newly diagnosed prostate cancer by the International Classification of Disease, Ninth Revision code (185.0). Data used for the analysis were derived from the MarketScan® Commercial Claims and Encounters and the Medicare Supplemental and Coordination of Benefits databases to longitudinally assess the inpatient and outpatient experience for men after definitive prostate cancer surgery from 2003 to 2006. These databases incorporate the health services of approximately 3 million employees, dependents and retirees in the USA with primary or Medicare supplemental coverage through privately insured fee-for-service, point of service, or capitated health plans. The MarketScan Commercial Claims and Encounters and Medicare supplemental databases are generally representative of the demographic makeup of the USA, although higher concentrations of MarketScan subjects reside in the south and midwestern areas of the USA than the general population [2]. The use of these data may lead to statistical differences when analysing outcomes by geographic region because of oversampling in the south and midwestern regions.

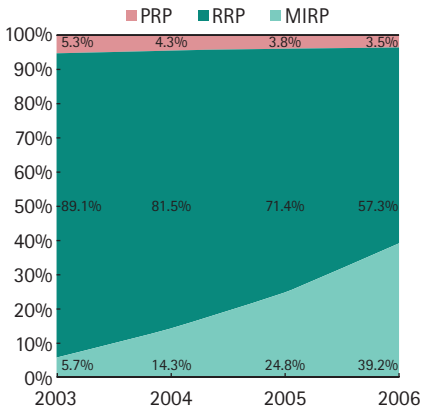
All enrolment records and inpatient, outpatient, ancillary and drug claims were collected. The study population consisted of persons with newly diagnosed prostate cancer who underwent radical prostatectomy between 2003 and 2006. The study population was restricted to those men who, in the year before initial cancer diagnosis, had no other cancer diagnoses or treatments. Study subjects were required to have at least one subsequent cancer claim (diagnosis or treatment) in the 3 months after initial diagnosis to ensure that the initial claim was not a follow-up visit for a patient in remission or a visit for a diagnosis to be ruled out. Men receiving prostate cancer surgery were identified using the Physicians Current Procedural Terminology Coding System, fourth edition: codes for perineal radical prostatectomy (PRP; 55810, 55812, 55815); RRP (55840, 55842, 55845) and MIRP (55866). During this period, there was no specific code for robotic assistance so laparoscopic and robot-assisted laparoscopic surgery could not be separated in this analysis.

The independent variables were as follows. Patient age at the time of treatment (<55, 55–64, 65–74, ≥75 years) was obtained from the enrolment file. Patient comorbidity was assessed using the Charlson index based on administrative data captured the year before treatment as has been previously described [3]. Geographic region was classified according to US Census Bureau regions (Northeast, Midwest, South, West).

We captured dependent variables of interest using relevant International Classification of Disease, Ninth Revision or Current Procedural Terminology, fourth revision diagnosis and procedure codes (Appendix) [1,4]. Hospital length of stay was defined as the number of days from admission to discharge during the initial surgical visit. Heterologous blood transfusions were included if they occurred during the surgical hospital admission. Perioperative complications were ascertained in the 30 days after surgery and included potentially life-threatening cardiac, respiratory, or vascular events; bleeding; and other events, such as renal failure and shock. Additionally, a MarketScan variable for death was assessed within 30 days of radical prostatectomy. Patients who underwent a reoperation within the first postoperative week were also examined. Anastomotic strictures were identified up to 6 months after surgery, as other studies have shown that these events typically present within 6 months of surgery [5]. Incision hernia repair was assessed in the year after radical prostatectomy.

Utilization rates for PRP, RRP and MIRP were examined from 2003 to 2006. We compared trends in patient characteristics and outcomes of interest by surgical approach through the study period using Cochran–Armitage trend tests, and univariate differences between treatment modalities were assessed with chi-square tests. Mean length of stay was compared with one-way ANOVA; the Wilcoxon rank sum test gave similar results, so for simplicity, we present the ANOVA. All analyses were performed in SAS 9.2 (SAS Institute, Cary, NC, USA).

FIG. 1. Rates of different radical prostatectomy surgical approaches over time: PRP, perineal radical prostatectomy; RRP, radical retropubic prostatectomy; MIRP, minimally invasive radical prostatectomy.



RESULTS

Use of MIRP increased from 5.7% in 2003 to 39.2% in 2006 and MIRP displaced RRP, which decreased from 89.1 to 57.3% (Fig. 1). Use of PRP decreased from 5.3 to 3.5% from 2003 to 2006 and it comprised a small proportion of all radical prostatectomies. Because PRP represented a small proportion of overall surgeries, we excluded PRP from further analysis, leaving a final sample size of 18 717 men.

Demographic data for men undergoing MIRP and RRP are shown in Table 1. Whereas most individuals were between 55 and 65 years of age, the MIRP population tended to be slightly younger than the RRP cohort ($P < 0.001$). There was geographic variability between the two groups, with MIRP more likely to be performed in the Midwest and RRP more likely to be performed in the South. There were no differences in preoperative comorbidity between the two surgical approaches. Because of these differences in region and age in the two treatment groups, we also performed analyses for the outcomes adjusted for region and gender, but the results were similar to the unadjusted results, so for simplicity, we present unadjusted results for the outcomes.

Over the 4-year period, the mean and median length of stay declined for men undergoing MIRP ($P < 0.004$, Table 2). Overall perioperative complications decreased from 13.8 to 10.7% ($P = 0.023$). This finding was

	MIRP		RRP		
	n	%	*n*	%	*P*-value
Age (years)					
<55	824	20.3	2725	18.6	<0.0001
55–65	2286	56.4	7995	54.5	
65–75	875	21.6	3588	24.5	
>75	67	1.7	357	2.4	
Region					
Northeast	366	9.0	1293	8.7	<0.0001
Midwest	1489	36.8	4249	29.4	
South	1411	34.8	5280	35.8	
West	759	18.7	3761	25.5	
missing	27	–	82	–	
Charlson index					
0	1387	73.2	7248	72.7	0.1861
1–2	254	24.5	1515	25.3	
≥3	10	2.3	61	2.1	
missing	2401	–	5841	–	

TABLE 1 Demographics of the study population from 2003 to 2006

MIRP, minimally invasive radical prostatectomy; RRP, radical retropubic prostatectomy.

TABLE 2 Temporal trends in minimally invasive radical prostatectomy complications and iatrogenic injuries

	2003 ($n = 287$)	2004 ($n = 704$)	2005 ($n = 1172$)	2006 ($n = 1889$)	*P*-value
Mean length of stay (days)	2.1	1.9	1.9	1.7	0.004
Median length of stay (days)	2.0	1.0	1.0	1.0	–
Heterologous transfusion	0.7	2.6	2.3	0.7	0.014
Any complication within 30 days*	13.8	13.5	14.2	10.7	0.023
Cardiac	1.8	1.0	0.8	0.7	0.105
Respiratory	2.9	2.6	2.4	1.9	0.171
Vascular/clot	0.4	0.9	1.3	1.6	0.045
Wound/bleeding	0.7	0.7	1.2	1.0	0.521
Genitourinary	3.3	4.3	4.1	2.5	0.049
Miscellaneous medical	6.2	4.5	4.9	3.7	0.063
Miscellaneous surgery	3.6	4.8	3.9	2.3	0.006
Overall iatrogenic injuries within 30 days					
Intestinal injury	1.5	0.1	0.4	0.1	0.009
Re-exploration	1.8	0.6	1.0	0.7	0.211
Overall iatrogenic injuries within 6–12 months					
Rectal repair (6 months)	1.5	1.4	1.4	0.5	0.0710
Incisional hernia repair (12 months)	1.2	2.0	1.9	–	0.622
Stricture (6 months)	6.8	7.0	5.9	6.0	0.407

*All values in percentages unless otherwise stated; trend for mean length of stay assessed with GLM, all other P-values are two-sided Cochran–Armitage Tests for Trend. *If patients had more than one complication type then this was counted as one complication. All trend tests are restricted to those individuals having adequate follow-up time to fully assess rates of complication. Hence, the n values at the top of the columns are the entire sample, whereas each row is drawn from a subsample of cases. Specifically, 30-day complications have a denominator of 3783, 6-month complications have a denominator of 2715 and 12-month complications have a denominator of 1651.*

driven by the reduction in genitourinary complications (3.3 to 2.5%, $P < 0.049$) and miscellaneous surgical complications (3.6 to 2.3%, $P = 0.006$). Over the study period, there was a decrease in iatrogenic intestinal injury (1.5 to 0.1%, $P = 0.009$). Decreases in iatrogenic rectal injury repair (1.5 to 0.5%), surgical re-exploration within 30 days of initial surgery (1.8 to 0.7%) and stricture formation (6.8 to 6.0%) were identified, but were not significant.

Over the same study period, mean length of stay for men undergoing RRP decreased from 3.2 to 2.9 days, ($P < 0.001$) and overall perioperative complications decreased from 18.1 to 14.6%, ($P = 0.007$, Table 3). This decrease in perioperative complications was the result of reductions in wound/bleeding complications, (2.0 to 1.1%, $P = 0.002$). No significant trend was seen in either MIRP or RRP groups for the rate of stricture formation or incisional hernia repair.

When comparing perioperative outcomes by surgical approach (Table 4), men undergoing MIRP vs RRP had a shorter mean hospital stay (1.8 vs 3.1 days, $P < 0.001$). Men undergoing MIRP also experienced a reduced overall perioperative complication rate (12.5 vs 17.1%, $P < 0.001$). This difference was significant for cardiac (0.9 vs 1.6%), respiratory (2.3 vs 4.4%), vascular (1.3 vs 2.1%), wound (1.0 vs 1.5%), miscellaneous medical (4.4 vs 5.8%) and miscellaneous surgical (3.3 vs 4.1%) complications. The rates of blood transfusions (1.5 vs 8.7%, $P < 0.001$) and anastomotic strictures (6.3 vs 12.8%, $P < 0.001$) were lower for men undergoing MIRP than in those undergoing RRP. Although stricture rates were lower in men undergoing MIRP than in those undergoing RRP, postoperative use of cystography was higher (35.7 vs 9.1%, $P < 0.001$) in those who underwent MIRP. Finally there were two 30-day postoperative RRP deaths in 2004 and one death in 2006 whereas there were no deaths within 30 days of MIRP during the study period.

DISCUSSION

Adoption of minimally invasive approaches to radical prostatectomy has significantly grown over the past decade as urologists have embraced the purported advantages of decreased length of stay and earlier return of baseline function [6]. However, as the

dissemination of this technology spread from high volume centres into the community there have been few reports that detail the perioperative complications associated with the new technologies in the community setting that balance these benefits [7–11]. Our study attempted to quantify these differences over a 4-year period of increasing adoption of MIRP and compared the outcomes to RRP performed over the same interval.

TABLE 3 Temporal trends in retroperitoneal radical prostatectomy complications and iatrogenic injuries

	2003 (n = 4513)	2004 (n = 4020)	2005 (n = 3375)	2006 (n = 2757)	P-value
Mean length of stay (days)	3.2	3.1	3.1	2.9	<0.001
Median length of stay (days)	3.0	3.0	3.0	3.0	–
Heterologous transfusion	9.2	9.5	9.7	6.7	0.004
Any complication within 30 days*	18.1	16.7	18.2	14.6	0.007
Cardiac	2.0	1.4	1.6	1.2	0.046
Respiratory	4.3	4.5	4.8	3.7	0.514
Vascular/clot	2.2	1.9	2.1	2.1	0.805
Wound/bleeding	2.0	1.5	1.4	1.1	0.002
Genitourinary	2.3	2.7	2.8	2.7	0.338
Miscellaneous medical	5.9	5.6	6.5	5.0	0.474
Miscellaneous surgery	4.6	4.1	4.3	3.3	0.022
Overall iatrogenic injuries within 30 days					
Intestinal injury	0.4	0.6	0.3	0.4	0.496
Re-exploration	0.1	0.1	0.2	0.1	0.762
Overall iatrogenic injuries within 6–12 months					
Rectal repair (6 months)	1.1	1.2	1.1	0.8	0.472
Incisional hernia repair (12 months)	0.9	0.8	1.3	–	0.159
Stricture (6 months)	13.1	13.1	12.4	11.9	0.186

*All values in percentages unless otherwise stated. *If patients had more than one complication type then this was counted as one complication. All trend tests are restricted to those individuals having adequate follow-up time to fully assess rates of complication. Hence, the n values at the top of the columns are the entire sample, whereas each row is drawn from a subsample of cases. Specifically, 30-day complications have a denominator of 14 665, 6-month complications have a denominator of 11 472 and 12-month complications have a denominator of 8824.*

Our study has several important findings. First, MIRP use increased through the study period with a concomitant decrement in use of RRP. The trend in diffusion of laparoscopic radical prostatectomy is faster than laparoscopic nephrectomy, which comprised <10% of all cases 5 years after initial description [12]. However, its adoption rate is less than that of laparoscopic cholecystectomy, which accounted for at least 40% of all cases 5 years after initial description [12]. Increases in MIRP appear to be correlated with a mirrored decline in use of RRP. Moreover, there was significant geographic variation in the use of competing approaches to radical prostatectomy, consistent with previous studies [1,13]. However, because our observational study oversampled the Midwest and South regions of the USA, further study is warranted to delineate potential confounders that may influence use and outcomes of MIRP or RRP in these regions.

Second, length of stay decreased for both MIRP and RRP during the study period but men undergoing MIRP spent significantly less time in hospital compared with those undergoing open surgery. While individual physician practice patterns may contribute to the length of hospital stay, our finding is consistent with that of other studies [11,14]. Duration of hospital stay is the primary determinant of hospital costs associated with radical prostatectomy in the USA [7], and the shorter length of stay may result in cost advantages despite higher intraoperative costs as a result of use of disposables, acquisition of a robot and longer operative times [7].

We found that the overall perioperative complication rate decreased over the 4 -year study period in both the MIRP and RRP populations. The MIRP group had a statistically significantly lower number of perioperative complications than the open surgical group. These findings contrast with single centre reports of similar rates of perioperative and postoperative complications for both open and minimally invasive surgical approaches [15–17]. This decrease in complications is closely related to the reduction in intraoperative blood loss, which is associated with a lower rate of cardiac complications. It has been suggested that the use of carbon dioxide insufflation and the resulting decreased venous blood flow and tamponade lead directly to a decrease in blood flow within the operative field and overall blood loss [8,18–20]. Intraoperative blood loss has been shown to be a predictor of perioperative complications in general, vascular and gynaecological surgeries as well as in radical cystectomy [21,22].

We report the first analysis of decreasing trends in overall iatrogenic injuries and, specifically, rectal injury and surgical re-exploration, over this study period for MIRP. The period from 2003 to 2006 was a time of rapid adoption and dissemination of the minimally invasive surgical approach, mostly through robotic assistance. Our findings may be representative of both increased experience of laparoscopic surgeons and the addition of new MIRP surgeons. The rates of iatrogenic complications during MIRP began to resemble those of RRP by the end of the study period. Further analysis of MIRP complications in the future will help clarify if there is equivalence between the two approaches or if the added technical benefits of MIRP will allow for reduced numbers of complications once more surgeons progress along the learning curve.

Our data also showed interesting findings with regard to delayed complications. Although it was not significant, we identified a decreasing trend in rate of anastomotic strictures after MIRP. Additionally, the overall rate of anastomotic strictures was half that of RRP, which is consistent with the existing literature and may reflect better visualization

TABLE 4 Comparison of overall complications and overall iatrogenic injury rates between radical (RRP) and minimally invasive (MIRP) radical prostatectomy

	MIRP (n = 4052)		RRP (n = 14665)		P-value
Mean length of stay (days)	1.8		3.1		<0.001
Median length of stay (days)	1		3		–
	n	%	*n*	%	
Transfusion	60	1.5	1309	8.9%	<0.001
Any complication within 30 days*	472	12.5	2334	17.1	<0.001
Cardiac	33	0.9	217	1.6	0.001
Respiratory	85	2.3	598	4.4	<0.001
Vascular/clot	49	1.3	280	2.1	0.003
Wound/bleeding	37	1.0	211	1.5	0.009
Genitourinary	127	3.4	357	2.6	0.013
Miscellaneous medical	166	4.4	792	5.8	<0.001
Miscellaneous surgery	126	3.3	566	4.1	0.024
All iatrogenic injuries within 30 days					
Intestinal injury	11	0.3	59	0.4	0.226
Re-exploration	31	0.8	15	0.1	<0.001
All iatrogenic injuries within 6–12 months					
Rectal repair (6 months)	30	1.1	126	1.1	0.976
Incisional hernia repair (12 months)	30	1.8	85	1.0	0.002
Stricture (6 months)	170	6.3	1466	12.8	<0.001
Cystography within 30 days	1352	35.7	1244	9.1	<0.001

*All values in percentages unless otherwise stated. *If patients had more than one complication type then this was counted as one complication. All frequency tests are chi-square, and are restricted to those individuals having adequate follow-up time to fully assess rates of complication. Hence, the n values at the top of the columns are the entire sample, whereas each row is drawn from a subsample of cases. Specifically, 30-day complications have a denominator of 17 460, 6-month complications have a denominator of 14 187 and 12-month complications have a denominator of 10 475.*

of the urethrovesical anastomosis during surgery [5,15,23–25]. The reduction in stricture disease yields potential cost savings through avoided additional procedures, emergency room presentation, and office visits for postoperative management.

We identified a decreasing trend in the use of cystography over our study period, although it was used more frequently in the MIRP patient cohort. Two reasons have been proposed for this. First, despite improved visualization during suture placement, the transperitoneal approach frequently used in MIRP does not allow for a tamponade effect to control urinary extravasation from the urethrovesical anastomosis. Therefore, cystography is used to confirm a watertight anastomosis before catheter removal. Second, there has been a trend to remove the Foley catheter earlier after MIRP procedures given good visualization of the anastomosis and the associated improvement in quality of life reported without an indwelling catheter for extended periods postoperatively. Because no preoperative, intraoperative or postoperative variables have been found to be predictive of urinary extravasation, cystograms have been used to confirm the safety of removing catheters earlier after prostate surgery [26]. Unfortunately, the persistent use of cystography results in an added healthcare cost; it has been shown that for high-volume surgeons, routine use of postoperative cystography is probably unnecessary after radical prostatectomy [27].

We found that MIRP results in higher rates of incisional hernia repair than RRP. This finding is different from those reported in the general surgery and gynecological literature, where open surgeries had an incisional hernia rate of up to 15% compared with 3% in laparoscopic surgery, and a higher recurrence rate of up to 54% compared with 19% for laparoscopic approaches [28]. This difference may be related to the extraperitoneal approach used in open prostate surgery compared with the intraperitoneal approach most commonly used in MIRP. Additionally, the use of multiple diameters, designs and manufacturers of laparoscopic ports introduces variability and inconsistency in the need for closure of deep fascial layers after port removal.

Our findings must be interpreted with regard to the design of the study. MarketScan data are designed primarily to provide billing information, not detailed clinical information. We also could not adjust for tumour characteristics such as tumour grade or stage between the surgical approaches, although it is unlikely that differences in tumour characteristics would influence perioperative complications, anastomotic strictures, or length of stay. However, these differences may potentially impact the ability to provide nerve-sparing during surgery if there were differences between groups. Surgeon volume could not be categorized as MarketScan comprises multiple health plans, each with its own unique encrypted identifiers that preclude aggregation. During our study period, there was no separate Current Procedural Terminology procedure code for robotic assistance during MIRP. Therefore, our categorization included surgeries performed with and without robotic assistance and further stratification and analysis was not possible. Several reports suggest that robotic assistance may shorten the learning curve for MIRP [29,30] but additional research is necessary to determine whether differences in outcomes exist between MIRP with and without robotic assistance. Finally, incontinence and impotence rates were not analysed because another study using similar data to capture erectile dysfunction and impotence has been met with scepticism [31]. The use of administrative data to quantify diagnoses of incontinence and impotence is less sensitive than self-assessment with validated instruments [32].

The increasing adoption of minimally invasive approaches to radical prostatectomy during the mid-decade has been associated with reductions in hospital stay, perioperative complications and iatrogenic injuries. In addition, the complication rate is lower for MIRP than for RRP over the same period. While individual physician practice patterns may influence lengths of stay and patient selection, increasing use of MIRP has

continued to reduce the morbidity associated with radical prostatectomy nationally.

CONFLICT OF INTEREST

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Abbreviations: **MIRP**, minimally invasive radical prostatectomy; **RRP**, retroperitoneal radical prostatectomy; **PRP**, perineal radical prostatectomy.

EDITORIAL COMMENT

TRENDS IN THE CARE OF RADICAL PROSTATECTOMY IN THE UNITED STATES FROM 2003 TO 2006

Minimally invasive radical prostatectomy has become the most common technique for prostate cancer surgery in the USA, and a growing trend has been observed in Europe as well. The technology is attractive to many patients and surgeon-advocates, but comes at an additional cost to our healthcare systems. So what is the return on our investment in new technologies to treat prostate cancer? The year 2009 was very interesting in the USA for this discussion for three reasons: (1) a year-long debate on healthcare reform and cost control; (2) a federally sponsored economic stimulus package that earmarked large grants for comparative effectiveness research (CER): and (3) the JAMA publication by Hu *et al.* [1] on the same topic but using the Surveillance, Epidemiology and End Results (SEER)-Medicare database.

The Hu *et al.* JAMA article gained widespread media attention partly owing to the findings that '*Prostate cancer patients who chose minimally invasive surgery . . . reported higher rates of long-term problems, including impotence and incontinence, according to one of the largest studies to compare outcomes to date*.' [2]. However, the authors used diagnostic and procedure codes to imply functional outcomes rather than validated surveys of patient-reported outcomes. Meanwhile, most objective outcomes discernible from an administrative database such as length of hospital stays, complications and anastomotic strictures were favourable to minimally invasive surgery. In the present study, these authors used a proprietary insurance claims database (MarketScanÒdatabase) to capture outcomes from men of all ages, and again found increased use of minimally invasive surgery and several improvements in outcomes. However, in the present paper, the authors now concede the limitations of using diagnostic and procedure codes in an administrative database to ascertain functional outcomes and have not performed a similar analysis to that in their JAMA article. We believe, therefore, that the conclusions from the present study are a fairer reflection of what we can learn from these large administrative databases.

Moving forward, our understanding of the CER of prostate surgeries should not be limited to case series of high-volume surgeons, as such studies may provide better quality data (including functional outcomes) but may be overly optimistic and not reflect real world results. Administrative databases may complement CER with their large populations from multiple institutions across various practice settings. Feasible questions to address can include comparisons of high- vs low-volume providers, and cost analyses. With the present paper and the JAMA publication, the authors have demonstrated the strengths and weaknesses of CER using administrative databases, and these lessons should be valuable for future research.

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REFERENCES

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2 **Rabin RC.** "Study Finds Pro and Cons to Prostate Surgeries." The New York Times; October 13, 2009